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Personal Healthcare Agents for Monitoring and Predicting Stress and Hypertension from Biosignals

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Abstract

We live in exciting times. The fast paced growth in mobile computers has put powerful computational devices in the palm of our hands. Blazing fast connectivity has made human-human, human-machine, and machine-machine communication effortless. Wearable devices and the internet of things have made monitoring every aspect of our lives easier. This has given rise to the domain of quantified self where we can continuous record and quantify the various signals generated in everyday life. Sensors on smartphones can continuously record our location and motion profile. Sensors on wearable devices can track changes in our bodies' physiological responses.

This monitoring also has the capability to revolutionise the health care domain by creating more informed and involved patients. This has the potential to shift care-management from a physician-centric approach to a patient-centric approach allowing individuals to create more empowered patients and individuals who are in better control of their health.

However, the data deluge from all these sources can sometimes be overwhelming. There is a need for intelligent technology that can help us navigate the data and take informed decisions.

The goal of this work is to develop a mobile, personal intelligent agent platform that can become a digital companion to live with the user. It can monitor the covert and overt signal streams of the user, identify activity and stress levels to help the users' make healthy choices regarding their lives. This thesis particularly targets patients suffering from or at-risk of essential hypertension since its a difficult condition to detect and manage.

This thesis delivers the following contributions: 1) An intelligent personal agent platform for on-the-go continuous monitoring of covert and

overt signals. 2) A machine learning algorithm for accurate recognition of activities using smartphone signals recorded from in-the-wild scenarios. 3) A machine learning pipeline to combine various physiological signal streams, motion profiles, and user annotations for on-the-go stress recognition. 4) We design and train a complete signal processing and classification system for hypertension prediction. 5) Through a small pilot study we demonstrate that this system can distinguish between hypertensive and normotensive subjects with high accuracy.

Keywords

[Personal mobile agent, physiological sensing, activity recognition, stress recognition, hypertension detection]

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Introduction

"We live in an information economy. The problem is that information's usually impossible to get, at least in the right place, at the right time."

– Steve Jobs

We live in a connected world. There are (in early 2016) over 2.5 billion smartphones [18], and 4.9 billion connected devices being used worldwide. 78.1 million units of consumer wearable devices [10] were sold in the year 2015 alone. Gartner forecasts [4] that by the end of 2016, connected devices in the realm of the *internet of things* will grow to a staggering number of 6.4 billion devices. Everything we do, from browsing to driving generate an immense amount of data about us - our mouse clicks generate data about our behaviour in the virtual world, while the sensors in our smart devices generate data about our activities in the physical world. This data

Navigating, visualizing and making sense of this vast amount of data is a challenging task. Especially when the data is regarding our health and wellbeing - the

Navigating this vast amount of data and making sense of it is a very challenging task. Data may be relevant, irrelevant or noisy. There is a need for intelligent technology which can sift through all this data and help us make decisions by providing us with meaningful, intelligible and actionable information “in the right place, at the right time".

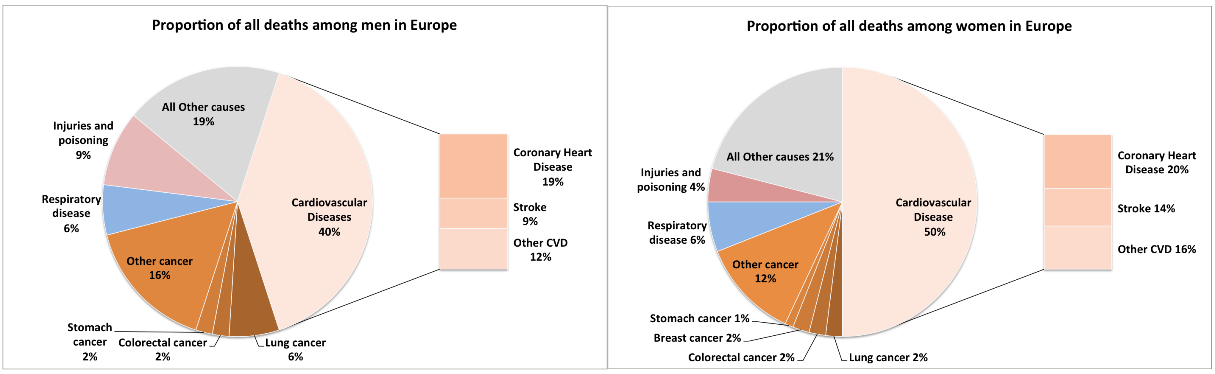
Traditional software systems help us accomplish tasks - in most cases they act as tools to support us. With the growing complexity of the information world, there is a need for them to evolve from mere tools we use, to assistants that help us to solve complex problems. An alarm application that wakes you up at a predefined time is a tool. A smart alarm which monitors your sleep state, gently wakes you up when you are in a light sleep stage, and also provides early warnings for sleep disorders becomes an *intelligent sleep assistant*. A map application that shows you the driving direction from point A to point B is a tool. An intelligent map which knows where you work, and provides you driving directions based on current traffic conditions and ensures that you are not late for work is an *intelligent driving assistant*. A news reading application is a tool, but an application which learns from the news you read and proactively provides you with the news articles which are most relevant to you is a *news curation assistant*.

Smartphones and wearable devices with their array of sensors have made the creation of such intelligent applications possible. These devices, which live with us, have opened up the opportunity to continuously monitor us, interact with us and learn about our preferences and behaviour. Intelligent applications may schedule our meetings and remind us if we are late; track our calorie consumption and help us stay on our diet; and even know how much we sit, walk, run or sleep and warn us if we are being lazy. Intelligent Virtual Assistants such as Siri [17] and Cortana [11] can perform simple tasks such as making calls, setting alarm, answering questions, and occasionally entertaining the user with smart and funny replies.

There is a great potential for applying these intelligent agents or assistants to healthcare management. Using data from wearable devices which can continuously monitor our physiology, these agents can keep an eye on our health. By interacting with the user and learning his or her behaviour, these systems can act as early warning systems. In this work we explore the applicability of such an intelligent agent for the detection and management of conditions such as stress and hypertension.

1.1 Motivation

Global increase in ageing population and incidence of chronic conditions such as hypertension has created new challenges for healthcare systems. According to the World Heart Federation there are at least 970 million people worldwide suffering from hypertension [19]. Hypertension, defined as a systolic blood pressure at or above 140 mmHg and/or a diastolic blood pressure at or above 90 mmHg is the single most important risk factor for stroke and other cardiovascular diseases. According to a report by the World Health Organization (WHO) [20] every year over 17.5 million people die from cardiovascular diseases alone. In Europe, cardiovascular disease is the most common cause of death; and every year over 4 million Europeans die of cardiovascular diseases. Over 40% deaths among men and 50% deaths among women are attributed to cardiovascular diseases (Figure 1.1).



(a) men

(b) women

Figure 1.1: Proportion of deaths due to major causes in Europe among men and women for 2015. No data available for Andorra. Source: WHO Mortality Database. [258]

Research suggests that most of these deaths are preventable through early intervention and lifestyle changes such as increase in physical activity [256], decrease in smoking [24], healthy diet [208], and stress reduction. To achieve these, a paradigm shift is needed in moving the focus of healthcare from a disease-centred approach to a wellness-centred approach.

Doctors can only spend a limited time with patients. Often, this time is not enough to gain a complete understanding of a patient's lifestyle and evaluate all the underlying causes and and risk-factors for predicting diseases. Checking physiological signals such as heart rate and blood pressure in the clinical setting may not always yield accurate results. Conditions such as **masked hypertension** (where a patient's blood pressure is $< 140/90$ mm Hg in clinical settings, but home blood pressure monitoring is in hypertensive range) or **white-coat hypertension** (where a patient's blood pressure is $\geq 140/90$ mm Hg in clinical settings, but home blood pressure monitoring is in normal range) increases the risk of erroneous diagnosis. Symptoms and conditions are reported by patient, and can suffer from bias in memory and perception. Patients often forget or mis-state certain critical conditions and symptoms, and over-emphasize others which they perceive as important. The use of technology can help to alleviate some of these problems.

Mobile health (mHealth) technologies such as remote monitoring, telemedicine, and home-based monitoring have become effective tools shifting the focus towards a more patient-centric healthcare. Adoption of wearable devices have provided the ability of continuous monitoring of physiological signals to provide a more complete timeline of the patient's health condition. Mobile applications are being successfully integrated into the clinical process for the continuous monitoring and treatment of chronic conditions such as diabetes, asthma and epilepsy. They are enabling easier disease management by improving medical adherence, symptom and condition tracking, patient awareness and early warnings. They are enabling a transition in the field of medical care from a reactive to a proactive approach of treatment. This new concept of proactive medical care-based smart health is characterized by 4 Ps - *Prevention, Participation, Prediction and Personalization* [268].

However, all these medical and technological advances produce a large amount of data. Continuously tracking, managing and analysing these large and high-dimensional datasets, identifying anomalous patient behaviour from the unstructured data, and applying individual patient specific interventions at the right time is a challenging task. This necessitates the development of smart medical care - where medical doctors and caregivers are supported by smart personalized digital health assistants. These digital health assistants should be able to support doctors to take more informed decisions about the patients by providing the most relevant information during the patient's visits, and also support the patient while out of clinic.

Digital health assistants have to include a synergistic combination of methodologies from fields of machine-learning and human computer interaction. Machine learning has the potential to learn about the behaviour and health condition of the individual patient. Applications of techniques from human computer interaction (HCI) can help lower the adoption barrier of these technologies into users' daily lives. Machine learning has made automatic detection of anomalies in the behaviour of the patients easier. Machine learning techniques have shown that they have the potential to improve medical adherence [73], can help in detecting hypertension [109], and even predict occurrences of heart attacks [245].

Another challenge is that in most cases these technologies are applied only once the disease has been diagnosed. Early intervention is one of the key factors for prevention of cardiovascular and mental diseases. A personal mobile health agent which can live with us, and collect, analyse and learn from our covert and overt signals provides enormous possibilities for continuous monitoring and early intervention. It can support us in our daily lives by facilitating an overall healthier lifestyle and well-being.

The work presented in this thesis is a small step towards this larger goal.

1.2 Thesis Goals

A key goal of this thesis is to present and demonstrate the utility of the Personal Agent in Healthcare. Personal Mobile Agent that can be used as a companion and live with the user. It can monitor the user's behaviour from the way he or she interacts with the world. Using wearable devices it can continuously monitor the physiological signals of the user, in order to provide early warnings. It can find relationships among physiological signals and discover underlying causes.

This thesis particularly targets patients suffering from or at-risk of essential hypertension. Essential hypertension is a critical condition, and managing it requires a holistic approach for prevention and cure. This thesis targets the identification of various parameters which affect the disease condition.

1.3 Thesis Contributions

The contributions of this thesis are at the intersection of the fields of human computer interactions, machine learning, and healthcare informatics. One overarching goal of this work is to take computational approaches out of laboratory and simulation settings and apply them to real world scenarios. All work has been done in the wild with real participants who carried on with their daily lives while using our system. The contributions are listed as follows:

1. An intelligent personal agent platform for on-the-go continuous monitoring of covert and overt signals from patients suffering from essential hypertension.

2. A machine learning algorithm for accurate recognition of activities from smartphone sensors. We demonstrate how audio signals can

improve the accuracy of activity recognition even at low sampling rates in on-the-go scenarios.

3. A pipeline that combines various physiological signal streams, motion profiles, and user annotations for on-the-go stress recognition.

4. Demon how such a such a system can help in identifying and predicting diseases such as Essential Hypertension and can be used to continuously monitor patients suffering from it.

5. A complete signal processing and classification pipeline for detection of essential hypertension. Through a pilot study we demonstrate that this system can distinguish between hypertensive and normotensive subjects with high accuracy.

1.4 Structure of the Thesis

The thesis outline is as follows:

Chapter 1 - Introduction - This chapter describes the research plan of the thesis. It presents the research approach, and the theoretical and practical motivations. It also highlights the goals and contributions of the thesis, and provides an outline for the rest of the content to follow.

Chapter 2 - Mobile Personal Agents - This Chapter provides an overview of the Mobile Personal Agents. It talks about what a mobile personal agent is, and its characteristics. It then discusses how such an agent can contribute to the field of healthcare. It reviews the various approaches which have been taken.

Chapter 3 - Covert and Overt Signals - This chapter discusses the various covert and overt signals which can be utilized for the digital and computational description of a person's lifestyle.

Chapter 4 - HEAL Platform - In this chapter we discuss the architecture of our Personal Healthcare Agent. We discuss the various design decisions, and the challenges.

Chapter 5 - Hypertension - In this chapter we discuss about the hypertensive disease state. We discuss about the conventional method of diagnosis. We also discuss about the management of hypertension and the challenges involved, and how we can solve those challenges. We discuss about the various physiological markers other than blood pressure and how we can use these markers to come up with a better diagnosis and disease management.

Chapter 6 - Activity Recognition - Classifying human activities is an important task. Identifying the amount of time spent in different activities such as walking, sitting or commuting can contribute to the recognition of stress in daily life. In this chapter we discuss how the various smartphone signals can be applied to build a robust activity recognition algorithm.

Chapter 7 - Stress Recognition - Stress is one of the key debilitating lifestyle factors. Detection and timely prevention of stress can help in preventing diseases such as hypertension. In this chapter we provide our stress recognition algorithm which uses the previously discussed HEAL Platform.

Chapter 8 - Hypertension Detection - In this chapter we discuss about our pilot study on Hypertensive patients. We discuss how by using a combination of various physiological signals we are able to distinguish them from normotensive subjects.

Chapter 9 - Conclusion - This chapter provides the closing remarks and the vision of the future work.

1.5 Publications Relevant to the Thesis

- Automatically classifying essential arterial hypertension from physiological and daily life stress responses. M.Danieli, A. Ghosh, E. Berra, C. Fulceri, F.Rabbia, F. Veglio, and G. Riccardi. ESH 2016 - The 26th European Meeting on Hypertension and Cardiovascular Protection, Paris, France, June 10 -13 2016
- COMPRENDERE L'IPERTENSIONE ARTERIOSA ESSENZIALE A PARTIRE DA COSTRUTTI PSICOLOGICI E SEGNALI FISIOLOGICI. XXXII Congresso Nazionale della Societa Italiana dell'Ipertensione Arteriosa 2015 Danieli, Morena and Ghosh, Arindam and Berra, E. and Rabbia, F. and Testa, E. and Veglio, F. and Riccardi, Giuseppe
- Detection of Essential Hypertension with Physiological Signals from Wearable Devices. Engineering in Medicine and Biology Society (EMBC), 2015 37th Annual International Conference of the IEEE, Ghosh, Arindam and Torres, Juan Manuel Mayor and Danieli, Morena and Riccardi, Giuseppe
- Annotation and Prediction of Stress and Workload from Physiological and Inertial Signals. Engineering in Medicine and Biology Society (EMBC), 2015 37th Annual International Conference of the IEEE Ghosh, Arindam and Danieli, Morena and Riccardi, Giuseppe
- Recognizing Human Activities from Smartphone Sensor Signals. ACM Multimedia 2014, Arindam Ghosh, Giuseppe Riccardi
- Collecting life logs for experience-based corpora. Interspeech, 2011 F. Francesconi, A. Ghosh, G. Riccardi, M. Ronchetti, and A. Vagin.

2

Intelligent Personal Agents

Baymax: Hello. I am Baymax, your personal healthcare companion.
Baymax: I heard a sound of distress. What seems to be the trouble?
Hiro: Oh, I just stubbed my toe a little. I'm fine.
Baymax: On a scale of one to ten, how would you rate your pain?

– Big Hero 6, Don Hall, Chris Williams, 2014

An intelligent personal digital agent that can live with us, assist us in our daily lives, and take care of us has been a dream of science fiction authors as well as computer scientists for a long time. From HAL [1], who would not open the pod bay door for Dave, to the more recent Baymax, which can help identify health problems, movie scripts abound with references to such intelligent agents. In recent years, developments in machine learning, artificial intelligence and mobile computing has taken this dream a few steps closer to reality. They have enabled putting intelligent agents into our browsers and our pockets. We seek help from machines as they ask "How may I help you?"; we have them monitor our lives, schedule our meetings and remind us to take medicines on time.

The concept of an intelligent agent has been around since the early

[1] movie :2001 a space odyssey

nineteen-nineties. In the Artificial Intelligent community, an agent is generally defined as [220]:

> *"an autonomous entity which perceives its environment through sensors and acts upon it through actuators."*

2.1 Types of Intelligent Agents

Intelligent agents have been adopted in a variety of domains ranging from task management to personal healthcare. Depending on their domain of application and the roles they play, they are referred by different names. Agents which assist the user in their daily tasks are aptly referred to as Assistants; Agents which accompany users in their daily lives and focus on *relationship building* with the user are referred to as Companions. The following are some of the broad types and categories of intelligent agents:

- Expert Systems: Expert systems are computer systems that emulate human problem solving skills by taking the experience of a human specialist or expert and transfering it to a computer system. Expert systems codify these experiences as a set of rules which are used to solve problems. They gained popularity in the late 1970s and 1980s and found applications in real time monitoring of system behaviour [136], analysis of sensor data for mineral exploration [126] and even speech recognition (the HEARSAY-II speech understanding System [90]). They were also applied in the field of computer-assisted medical decision systems. The*EXPERT* a system from mid 1970s, [207] was an expert system which simulated clinical cognition and applied it to the treatment of eye diseases. The SMH.PAL [135] was another expert system which was used to identify interventions for students with severe disabilities.

  Training an expert system required the acquisition of a large amount of knowledge from human experts. The underlying assumption was that the knowledge of the experts in a domain consisted of a set of rules and by identifying these rules, this knowledge could be transferred from the *experts* to the *system*. This task of identifying and transferring the knowledge faced two important challenges: a) Acquiring knowledge from human experts could not be performed fast enough, and hence posed as a major hurdle to the growth of this field. b) The transferred knowledge in the form of rules was often brittle - the system could not robustly tackle problems which deviated from the set of rules. Due to these challenges, by early 1990s, interest in expert systems dwindled.

- Information Management Agents: The world wide web has made the entire information of the world available at our fingertips. However, organizing all this information and effectively and easily seeking out the most relevant one at the right time can often be very challenging. Intelligent Agents systems can help us navigate through the information space and effectively extract, summarize, and present the required information. Intelligent agents have been designed for extracting information from the web, managing personal information of individuals, and for managing collaborative information involving multiple participants.

  Intelligent agent which supports the acquisition, organization, maintenance, retrieval, and sharing of personal information in our daily lives are called personal information management agent (PIMA). The goal of a personal information management agent is to facilitate the easy management of information such as contacts, calendars, and to-do lists. Recent studies with personal information management agents [278, 249] demonstrate that they can improve ease of use of a system, and decrease the cognitive load of the user.

  Information management agents are also common in the travel and tourism domain where smart tourist assistants can help in every aspect of a tour including providing personalized recommendations of what to visit [34], scheduling and planning a route for the tour [262], as well as acting as intelligent context-aware tour guides [21, 62].

  Systems such as the IBM Watson cognitive computing system [7] can acquire and manage information from diverse sources. IBM Watson has been applied to question answering [36], information extraction, discovery and management from diverse streams [8], and even clinical studies [9].

- Task Execution Agent: Often aptly referred to as an assistant, the main goal of a task execution agent system is to assist the users in performing their daily tasks. Intelligent assistants have been deployed in different domains to solve problems such as organizing emails [233, 100], scheduling meetings [260], managing time [197, 193], fetching and summarizing information such as news and communication [41] among others.

  The CALO (Cognitive Assistant that Learns and Organizes) [1] funded by DARPA aimed at providing the users assistance in organizing and prioritizing information from emails; automate routine tasks such as travel authorizations for the user; mediate human communication as the user interacts with others 2.1. One of the spin-offs of the CALO project was the Siri intelligent software system which powers Apple's Siri conversational agent. Siri can set reminders and calendar entries, make calls and send messages, and find directions for the user.

  Recently commercial intelligent assistant applications such as x.ai 2.2, slackbot, and google inbox use machine learning to perform simple tasks such as automate meetings, reply to emails, manage expenses and even book restaurant tables.

- Personal Monitoring and Lifelogging Agents: Lifelogging is the process of digitally capturing (logging) different aspects of our lives. Dodge and Kitchin [79] defines life-logging as *"... a form of pervasive computing consisting of a unified digital record of the totality of an individual's experiences, captured multimodally through digital sensors and stored permanently as a personal multimedia archive"*. This continuous massive logging of personal data has given rise to the concept of "Quantified Self" [254] which involves two steps: 1) gather all the data about oneself, and 2) analyze and quantify all this data.

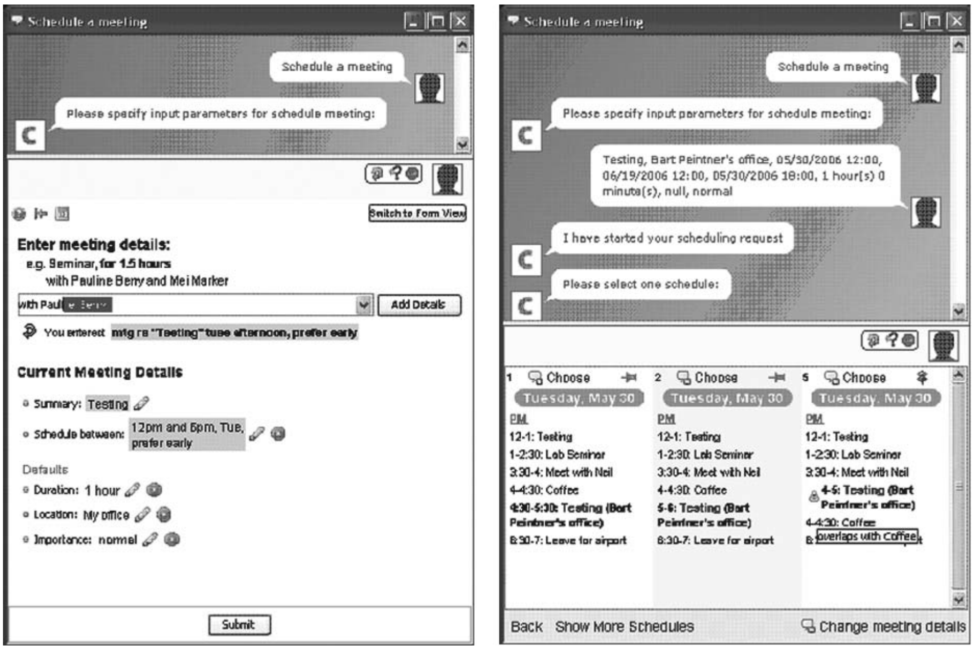


Figure 2.1: Project Execution Assistant (PExA) from the CALO project (2007)

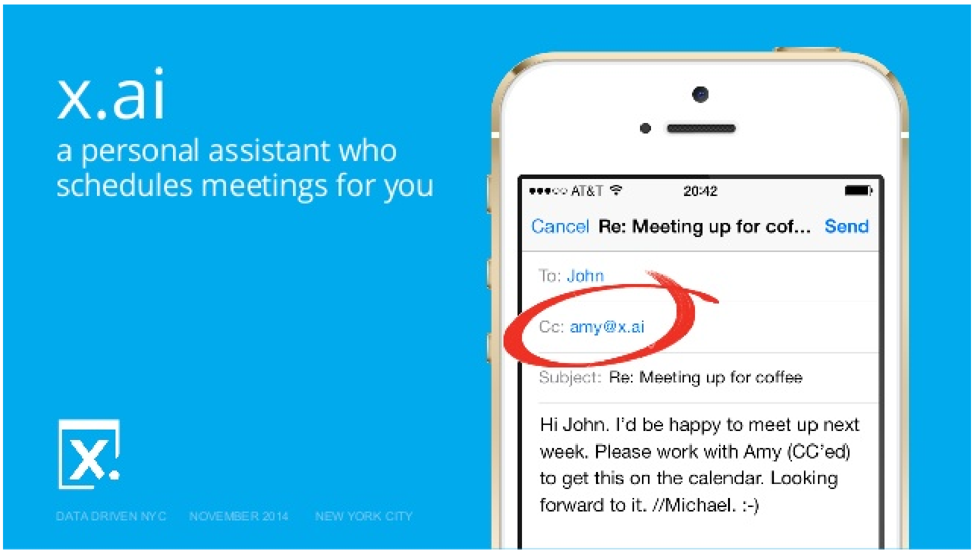
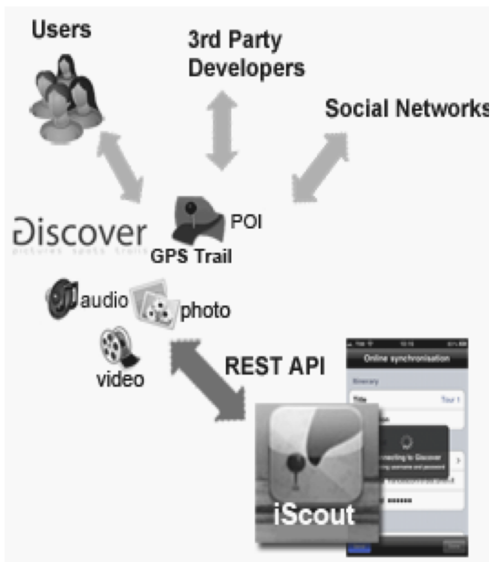


Figure 2.2: X.AI - an assistant for scheduling meetings (2015)

The goal of the quantified self movement is to be able to act upon the information which is tracked to improve one's life. A variety of personal attributes and signals may be tracked and analysed using a variety of devices. The trackable signals and attribues include weight, energy level, mood, sleep quality, health, and daily activities, heart rate among others. The objective of quantifying oneself can range from general tracking of various signals to improving physical and mental performance to creating digital memories.

Intelligent lifelogging agents can assist in signal acquisition, storing, analysis and retrieval. The iScout agent [99] is a lightweight lifelogging assistant for acquisition, sharing and annotation of experience-based corpora via mobile devices. iScout allows the collection and curation of memories and experiences in everyday lives. The collected memories can be browsed, searched, and annotated with speech and notes for later reference.

(a) iScout Mobile Agent

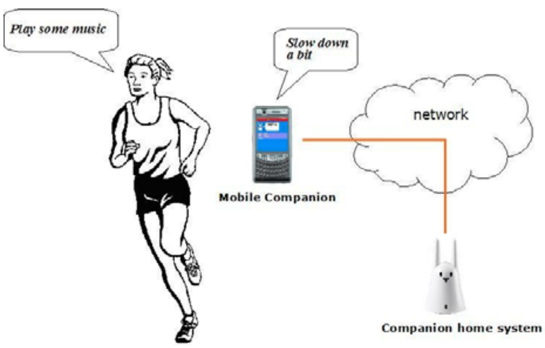


(b) iScout Server

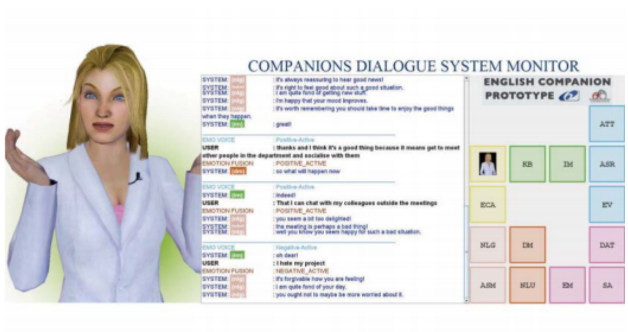
Figure 2.3: The iScout Lifelogging Agent can be used for collecting, organizing and curating memories. a)The iScout client is capable of recording and tracking several different kinds of signals. b) The iScout server integrates with various services which can be used for analysis and visualization of the data.

- Relational Agents: Relational agents, often referred to as *Companions*, are computational entities designed for *relationship building* with a user. Relational agents can interact with the user through conversation (voice or text), learn about the user's needs and preferences, and form long-term relationships with the user. They learn about the emotional and physical state of the users they accompany.

The EC-funded COMPANIONS project developed a conversational relational agent prototype system which acts as a health and fitness companion [248] . The Companion (Figure 2.4a) has a stationary embodied home component, and a mobile component which runs on a smartphone, and can be used during physical exercise to track the distance, pace, duration, and calories burned. The CIRDO [46] is Smart Companion project which aims to ensure safety at home to enable seniors to "age in place". The project consists of a smart companion that can live with the user and uses audio and video processing to detect critical events such as falls, and other situations of distress. The MemoryLane [184] is a mobile intelligent storytelling companion for the elderly which composes excerpts selected from a lifetime of memories and conveys these past memories as stories. The How Was Your Day (HWYD) Companion [57] is an embodied conversational agent which provides advice and support to the user about his or her everyday problems (See Figure 2.4b).



(a) COMPANIONS Project



(b) HWYD Project

Figure 2.4: The a) Health and Fitness Companion from COMPANIONS project and b) The How Was Your Day(HWYD) Companion (HWYD) are both examples of virtual companions which live with the user

2.2 Characteristics of Intelligent Agents

Over the course of the last two decades Agents have been adopted into real-life applications. The ability to perceive and to act are the two fundamental characteristics of intelligent agents. However, depending on the domain of application and the needs of the system, certain additional characteristics and qualifiers have started to define today's intelligent agents. Qualifiers such as *Mobile*, *Intelligent*, *Virtual*, *Personal* , *embodied*, *conversational* have been used to define these agent systems. It is important to clarify these terms before proceeding.

1. ***Mobile:*** In the history of computer science *mobility* has been used in different contexts at different times. In the early days of AI, there was a great interest in *logical mobility* of software components. A mobile agent was used to refer to a software whose code could be relocated from one software system to another. Over time, with the introduction of client-server systems, such software mobility is no longer a challenge. We are interested in mobility as used in the context of physically mobile systems related to the use of untethered mobile devices as computational units. This *physical mobility* of devices opens up unique opportunities in terms of autonomy and sensing. It also introduces new challenges due to added noise from inaccuracies of the sensors.

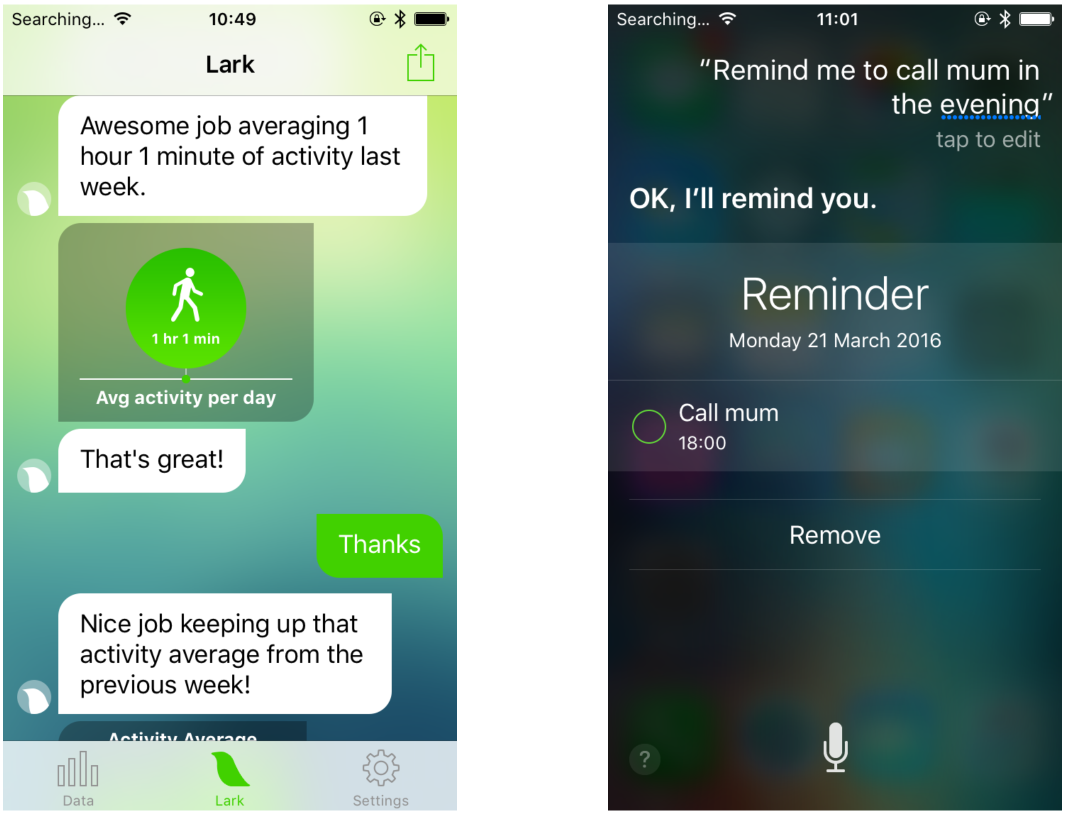
2. ***Intelligent:*** An intelligent agent is one which can achieve its objectives and goals. It can act autonomously and take decisions on behalf of its user. One important characteristic of an intelligent agent is its *context-awareness*. The knowledge of the user's context is very important while taking decisions on behalf of the user.

3. ***Interactive:*** A Personal Agent system should be able to interact with the user and the surroundings. This interaction is an important factor for the agent to learn about the user. This interaction could be either *reactive* or *proactive*. In a reactive interaction paradigm the agent responds (reacts) to user's queries and requests. Most agents

that answer questions or provide reminders and perform tasks on the basis of the user's request fall under this category. In the proactive form of interaction, the agent decides to initiate the interaction. This could be in the form of questions to elicit information from the user or in the form of notifications or information which the agent deems important for the user.

4. ***Virtual:*** An agent is a virtual piece of software. While there is research on how to embody agents, and in some cases agents have been embodied within physical objects, the agent itself is accepted to be a virtual entity.

5. ***Personal:*** A personal agent is one which can adapt its own behaviour based on the user's preference and behaviour. Just as a human agent or assistant learns about his or her employer over time, the digital counterpart should also be able to learn about the user, and customize and personalize interactions. This personalization could be as simple as learning to turn off the ringer when the user reaches work, or knowing what kind of food to suggest to user based on the user's restaurant check-ins, or being able to identify what increases user's stress based on changes in his or her physiological signals.



(a) Lark (b) Siri

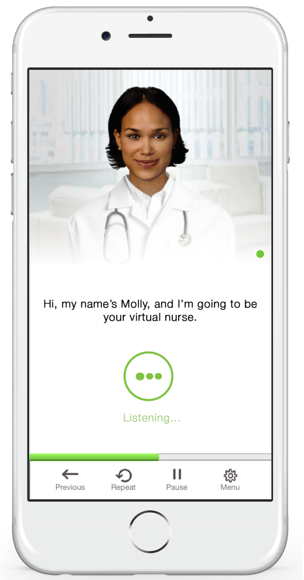
Figure 2.5: Conversational Agents like Lark and Siri can engage user's in conversation. They can accomplish tasks and elicit information

6. ***Conversational:*** A conversational agent can interact (converse) with the user through natural language. This interaction can be either voice based, text based, or through a multi-modal interface. Conversational Agents can understand commands and queries in natural language, and respond back with answers. These queries could be simple information extraction tasks such as "What is the time in New York now?" or commands like "Remind me to call mom in the evening". Conversational agents have recently gained popularity and have seen applications in e-commerce, travel booking, finance, and mobile applications. They can be used to replace human agents for answering queries for website visitors, or automating tasks in call centers.

   Conversational Agents like Lark [12] (Figure 2.5a) elicit information from users to learn about the user (thus leading to improved personalisation). Smartphone based agents such as Apple's Siri [17] (Figure 2.5b) or Microsoft's Cortana [11] can tap into the various sensors of the mobile phone and thus provide contextual answers to the user. For a query like "Which is the best Indian restaurant in the city", smartphone based conversational agents can use the location sensor on the phone to disambiguate the "in the city".

7. ***Embodied:*** Embodied agents (Figure 2.6) are agents that have a perceivable digital representation. This digital representation which may be anthropomorphic in nature is designed to be lifelike or believable with the ability to act or react to human users. Embodied agents are designed to emulate the experience of face-to-face conversation. Embodied conversational agents can be enriched by a variety of facial expressions, gestures, and postures which can make the conversation more lifelike.

(a) The SpeaktoIt Embodied Agent



(b) Molly from Sense.ly

Figure 2.6: Embodied Agents a) The SpeaktoIt Embodied Agent - emulating face-to-face conversations b) Molly the Virtual Nurse from sense.ly

2.3 Components of Personal Agent Systems

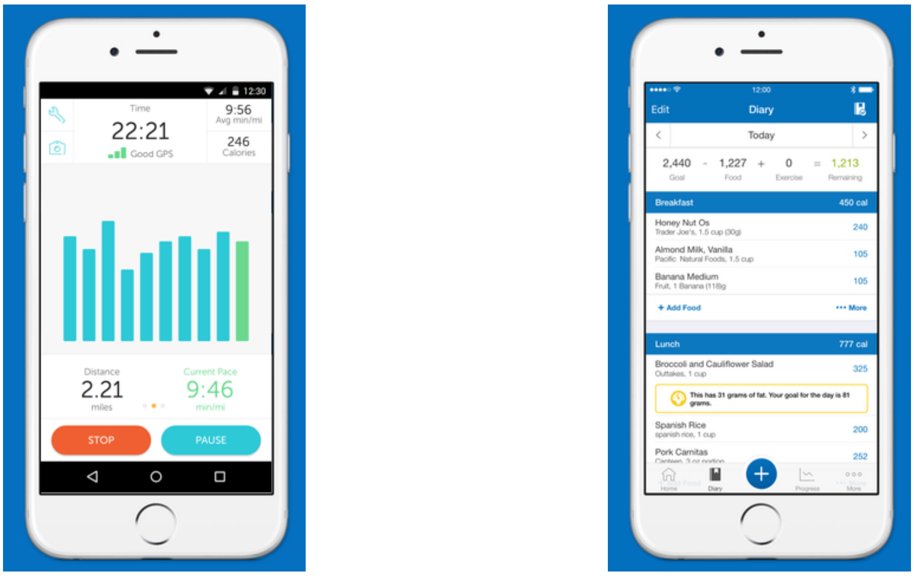
2.3.1 Smartphones

Until recently development and deployment of such an agent was limited by the low physical mobility and connectivity of computing systems. In the last decade, smartphones with their ever increasing physical mobility, connectivity, computing power and on-board sensing capabilities have successfully removed these limitations. Their ubiquity and penetration into our lives have made them perfect delivery vehicles for such intelligent assistive systems.

Smartphones have become an indispensable part of people's daily lives. They have combined and compacted the power of everyday objects such as cameras, maps, calendars and schedulers and placed them all in a single device in the users' pockets. They have also become powerful programmable computational platforms that allow their capabilities to be augmented through applications (called Apps) which can be downloaded from online application stores.

Smartphones have a plethora of sensors embedded in them. Most smartphones come equipped with at least an accelerometer and a gyroscope on them. These sensors can be used to detect the motion of a user. This can be used to identify whether a user is stationary, walking, running or travelling by a vehicle. The Geographical Positioning System (GPS) sensor, can pinpoint the user's location. The ambient light sensor can be used to detect the light around the user, which can be used to automatically adjust the brightness of a smartphone screen, or track when a user usually goes to sleep. The bluetooth, and wifi sensors can sense the network around the user. This information can be used to identify who the user is with. Even the simple microphone sensor can be used to detect ambient noise and to profile whether the user is alone, or in a crowded place. Apart from this, the smartphone can connect to wearable devices which can monitor a range of physiological signals of the user such as his or her heart rate, skin temperature, and galvanic skin response. These signals can be used to track different dimensions of a user's mental and physical health and wellbeing, and provide deeper insights into his or her lifestyle.

Smartphone applications regularly utilize the signals from these sensors to intelligently track and monitor users. Smartphone applications such as Human [6] and Runkeeper [16] (Figure 2.7a) can keep track of our activities; applications such as Myfitnesspal [15] (Figure 2.7b) and Lark [12] can keep us on track towards our weight loss goals by rating the food we consume; Google Now [5] can remind us about our upcoming meetings and inform us when our bus is late; and Siri [17] or Cortana [11] can answer questions, set reminders, hold limited conversations, and occasionally even demonstrate humor.



(a) Runkeeper (b) MyFitnessPal

Figure 2.7: Commercial Smartphone Agents to keep track of activity and nutrition. a) Runkeeper keeps track of the activities such as walking and running b) MyFitnessPal keeps track of nutrition content and calories consumed

2.3.2 Wearable Sensing Devices

Wearable sensing devices (Figure 2.8), a recent addition to the health and fitness market consist of a range of devices including health and fitness trackers, activity monitors, and physiological sensors. Wearable sensors can monitor a variety of health and fitness parameters and signals which can be used to understand both mental and physical health of the user wearing them. Some of the typical parameters that can be monitored are:

1. ***Activity:*** Most wearable devices at least serve as activity and fitness monitors. Because of this, the tri-axial accelerometer is the most common sensor present on these devices. Similar to their smartphone counterpart, this sensor can measure movement (acceleration along the three axes) to determine the activity profile of the user.

2. ***Heart Rate:*** The measurement of heart rate can provide interesting information about an individual. Heart rate is an important determinant for health and disease. It is an indicator for stress [37, 141], hypertension and cardiovascular diseases. Reduced heart rate recovery after exercise has been shown to be an indicator of increased risk for death from cardiovascular disease [259, 201].

3. ***Skin Temperature:*** Thermo-regulation is an important physiological characteristic. Continuous high skin temperature can often be an indicator of disease. The variation in body temperature can be used to detect the symptoms of mental stress that might lead to various health conditions, including stroke, heart attacks and shock.

4. ***Electrodermal Activity:*** Electrodermal Activity or Skin Conductance is the change in the electrical property of the skin. The conductance of the human skin varies with changes in the moisture level (due to perspiration). Since the sweat glands are controlled by the sympathetic nervous system, skin conductance is used as an indicator for psychological and physiological arousal.

5. ***Electroencephalograph (EEG):*** Although not a common sensor in wearable devices, measurement of EEG is becoming popular for brain sensing experiments. EEG detects the electrical activity of the brain and can be used to measure concentration, stress, and workload among other things.

(a) Apple Watch

(b) Empatica E4

Figure 2.8: Wearable Devices can keep track of physiological signals. The Apple watch can measure activity and heart rate. The Empatica E4 can measure heart rate, electrodermal activity, and skin temperature.

2.3.3 Internet of Things

From refrigerators to parking meters the internet of things is turning everyday objects into smart systems which can sense their surroundings and connect and communicate with each other. While wearable devices help intelligent agents learn about the user, the internet of things can help an intelligent agent learn about the environment of the user.

An intelligent agent can connect to the smart fridge in a user's home to identify what the user is eating in order to ascertain if the user is following his diet. It can connect to data coming from traffic sensors to suggest a less busy route to the user's office. It can switch on the smart thermostat at home when it detects that the user has left office. It can connect to the environmental sensors in the park where the user runs every morning to identify the pollution and pollen level, and notify the user accordingly. Intelligent agents can utilize the sensing capabilities of the internet of things to improve the everyday convenience and safety of a user.

2.4 Healthcare Agents

Healthcare is a diverse and complex system with knowledge, decision-making, and care-coordination being distributed and shared among different entities ranging from practitioners, patient-families and patients themselves. Traditional treatment plans and understanding of patient health risks are based on a limited subset of data - historical data, patient and family reports, and clinical test data. While advanced data analytic and machine learning techniques are already popular in fields such as retail, finance and telecommunication, they have been quite slow to enter the domain of patient management. Intelligent agent based systems can be applied to healthcare to increase quality and efficiency of care management, reduce cost of healthcare delivery, and improve compliance and patient management.

Certain characteristics of intelligent personal agent systems make them highly desirable for applying to the healthcare domain. They enable the application of personalized medicine to patient care. **Personalized Medicine** blends diverse information sources, including genetic profile, behavioural and historical data with clinical reports. Combining all these diverse data sources ensures that medical treatments can be tailored to the individual characteristics of each patient. Social, environmental, and activity data can be highly indicative of the health of an individual. It has been shown that in the case of mental diseases such as depression, individual responses vary widely to specific treatments. This requires that patients are closely followed to detect how they are respond to treatment. While self-reporting and diaries can help the doctors obtain records of a patient perception about his or her disease, combining these records with physiological signal and other sensor data can help generate a more complete disease timeline and can provide a better prognosis. A recent study [224] by Saeb et. al demonstrated that it is possible to predict the severity of depressive symptoms by monitoring the mobile sensor data such as location and phone usage.

Intelligent agents can be applied at each stage of health care - for the chronically ill - to manage their condition in their everyday lives; for the sick - while they are hospitalized; for a discharged patient - for managing post-discharge rehabilitation. Intelligent agents can also be helpful in preventive care for providing early warnings.

- **Chronic Condition Management** - Life-long conditions such as hypertension, diabetes, asthma and mental health conditions are presenting new care-management challenges. Chronic conditions require continuous monitoring and care management which can often be overwhelming for patients suffering from such diseases. There is a need for applying technology for helping such people to self manage their condition and stay autonomous in their home environment.

  A number of personal monitoring technologies have been suggested for improving chronic care management. For most patients, recording their food and medication intake, and activity level is a regular part of management. For patients suffering from hypertension, doctors recommend regular recording of blood pressure for disease tracking. For diabetic patients, blood sugar monitoring is a regular part of their disease management regimen. For patients with mental health problems, psychologists often suggest expressive writing techniques such as end-of-the-day diary writing to record their daily experience and activities.

  Patients are already burdened by the complications of their disease. There is a need to simplify the monitoring and recording process. The need of the moment is simple, unobtrusive continuous monitoring for better care management. In recent years there has been a lot of research to simplify monitoring and management. One important factor for chronic condition management is personalization of the management and therapy. Each therapy depends on a lot of individualized factors and an intelligent agent system which can learn about the individual patient's characteristics and behaviour can improve care.

  The MONARCA system [32] showed that use of an intelligent personal health monitoring and feedback agent for patients suffering from bipolar disorder improved patient experience, disease awareness and self-treatment. They demonstrated that a smartphone based companion system improved monitoring and self-assessment adherence compared with paper-based forms.

- **During Hospitalization Care** - The experience of being hospitalized can be extremely stressful for a patient. Improving patient comfort and satisfaction is often a necessary factor for better treatment and early recovery. In this setting intelligent agents can be applied in healthcare systems to improve patient experience. Evidence suggests that informed patients who understand their clinical situation are more adherent to their care plans and engaged in clinical decision-making [112].

  A study by Wilcox et al. [271] showed that in emergency departments patient comfort and satisfaction can be greatly improved by keeping them informed of their health status and treatment progress. Vardoulakis et al [209] showed that this can be achieved by using an interactive mobile agent that can increase patient engagement.

  Bickmore et al. in [38] demonstrated “Hospital Buddy" (Figure 2.9) - a virtual agent designed to chat with patients about their hospital experience. The buddy integrated with multiple sensors to make the agent aware of events in the hospital environment and more aware of the status of the patient. This information was used by the agent to interact with the patient to converse about his or her health and daily experience during the hospital stay. They showed that this interaction greatly enhanced a patient's hospitalization experience, and provided rich companionship to the patient. In [39] they demonstrated that such an agent was also useful for educating and counseling patients with inadequate health literacy at the time of discharge.

- **Post Discharge Care** - Post discharge care is one of the most complicated and critical step in a patient's recovery process. Patients are extremely vulnerable in the early days after discharge and this can often lead to relapse and re-hospitalisation. Engaging patients

Figure 2.9: A patient interacting with the **Hospital Buddy** - this greatly enhanced the patient's hospitalization experience, and provided rich companionship to the patient

and families in the discharge planning process can help to make this transition in care safe and effective. For psychiatric patients, continuous monitoring during post-hospitalization phase can help to increase patient safety, and recovery while preventing relapse. For cardiovascular patients, post-discharge observation might often be necessary for proper rehabilitation.

Personal health monitoring agent systems which can automatically monitor and collect heart rate, electrocardiogram (ECG) and blood-oxygenation levels can support the rehabilitation process of patients after heart surgery or recovering from a heart attack. Such agents can employ algorithms for analysis of physiological activity based on the heart rate and other physiological signals thus providing advance notice of any critical events. For patients with mental health issues, these devices can track physiological signals and detect any signs of excess stress or agitation.

- **Preventive Management** - Personal agent systems which can continuously monitor the health of an individual is not only beneficial for the sick. It can also be effective in maintaining the wellness of an individual. Preventive health management is an important factor for obesity control, fall detection, stress reduction, and cardiovascular monitoring. Continuous monitoring of activity levels can be used to motivate a user to get an adequate level of exercise or sleep. Continuous monitoring of eating habits can be used to motivate a user to eat healthy. Monitoring of physiological signals such as heart rate, blood pressure, or skin conductance can help a user avoid stress.

Mobile Personal Agents can monitor, and learn about our health and behaviour. They not only have the potential to be assistants to help us, but also guardian angels who can look after our health, and provide us advance warnings. In this work we explore how we can apply mobile personal agents for monitoring stress and hypertension. We demonstrate the potential of mobile personal agents for out-of-clinic monitoring. We show that they can be used to detect and continuously monitor the activity and stress levels of patients. By interacting with the patients to elicit information, they also enable the patients to be more engaged in their own care.

2.5 Challenges for Personal Agents in Healthcare

Deploying personal agents in healthcare scenarios have their own challenges. As soon as the sensing environment changes from controlled to on-the-go, personal agents have to deal with challenges of noisy signals, as well as be aware of the users' contexts in order to interact with the user. Some of the challenges, and the approach used in this thesis to deal with these challenges are explained as follows:

- In-the-wild testing - Most agent systems are built with data and models collected in controlled environments. While these might yield accurate results in controlled experimentation, they fail in realistic settings and their usability in real-life on-the-go scenarios are greatly diminished. In our work, to avoid this serious limitation, all the data was collected in real-life on-the-go scenarios.

- Learning from noisy physiological signals - Physiological signals such as heart rate and electrodermal activity are highly susceptible to noise and artifacts arising due to motion, pressure or nervous fidgeting. Learning from these individual signal streams is not effective. In this work we solve this problem by applying signal processing techniques to reduce artifacts and then combining different signal streams for learning.

- Modeling the activity profile of the user - In healthcare scenario, it is very important for a personal agent to model the context of the user. Identifying the physical context of the user (whether he is walking, driving, sleeping) can help the agent disambiguate other signals. An increase in the patient's heart rate while sitting needs to be interpreted differently that an increase while he is on a run. In our work our Intelligent Agent uses the accelerometer signals of the user's smartphone to model the user's activity profile. We identify six different activity profiles of the users - walking, standing, sitting, travelling by bus, travelling by train, driving/travelling by car.

- Eliciting information from the user - Eliciting information from the user is always a challenge. In our work we use a multi-level elicitation strategy which combines free text and speech-based annotations, with directed questions and list-based annotations.

2.6 Conclusion

In this chapter we briefly explored the history and evolution of intelligent agents. We highlighted the characteristics of such agents and described the components that make up a personal agent system. Intelligent agents have been applied to the healthcare domain for improving the experience of patients during and after hospitalization. In combination with wearable sensors, an intelligent agent can also be used to continuously monitor and manage chronic conditions. In the following chapters we will explore how we use this to detect stress and manage patients suffering from hypertension.

3

Hypertension

Hypertension is one of the most prevalent diseases of the modern world. According to a recent report by the World Health Organization (WHO) [204], hypertension affects more than 40% of the adults over the age of 25. In 2008 over 1 billion people worldwide were found to be suffering from hypertension. If left untreated it can lead to serious cardiovascular and cerebrovascular complications, and even death due to renal failure [215], heart attack [50], or stroke [195]. Every year there are over 9.4 million deaths from heart disease related to hypertension [204].

Hypertension has been called the “silent killer" because at early stages it is usually asymptomatic apart from a rise in blood pressure. Since most otherwise healthy people do not regularly check their blood pressure, due to the lack of early overt symptoms, hypertension can go undetected for years. By the time symptoms start appearing, significant damage to the heart, arteries and other organs is already underway. Since blood pressure is one of the only observable early predictors of this disease, physicians often recommend regular monitoring of blood pressure to enable early diagnosis.

3.1 What is Hypertension?

The cardiovascular system, which consists of the heart, veins, arteries and blood vessels is responsible for transporting oxygen and nutrients to all the tissues in the body. The pumping action of the heart which circulates the blood around the body determines the cardiac output (CO). The cardiac output, along with the systemic vascular resistance (the resistance offered to the blood flow by the peripheral circulation) determines the blood pressure.

Blood pressure can be measured using either a conventional sphygmomanometer and stethoscope or an automated electronic blood pressure monitor 3.1. It is recorded in terms of millimeters of mercury (mm Hg) and is reported as a pair of two numbers. The higher number, called the **systolic blood pressure** (SBP) is the highest blood pressure in the blood vessels which occurs when the heart contracts. The lower number, called the **diastolic blood pressure** (DBP) is the pressure in the blood vessels when the heart distends. Normal adult blood pressure is defined as a systolic blood pressure of 120 mm Hg, and a diastolic blood pressure of 90 mm Hg.

(a) Conventional Sphygmomanometer

(b) Automatic Electronic BP Monitor

Figure 3.1: Blood pressure can be measured using either a a) conventional sphygmomanometer and stethoscope or b) an automatic electronic blood pressure monitor.

Hypertension refers to an increase in the systolic and/or diastolic blood pressure. There are two main types of hypertension - primary hypertension and secondary hypertension. **Primary or essential**

hypertension is defined as persistent high blood pressure without any identifiable causes. In primary hypertension, the resting systolic blood pressure (SBP) is $\geq$ 140 mm and/or the diastolic BP (DBP) is $\geq$ 90 mm Hg. Primary hypertension accounts for 90% cases of hypertension.

When the high blood pressure is due to other underlying disease factors such as primary aldosteronism, renovascular disease, or obstructive sleep apnea, it is called **Secondary Hypertension**. Controlling or curing the underlying medical condition usually results in blood pressure reduction in case of secondary hypertension.

3.1.1 Complications Arising from Hypertension

Hypertension greatly affects the cardiovascular system. Most of the changes in the organ system happens because the human body tries to adapt to the increase in blood pressure. This elevated blood pressure often leads to structural changes to the body. Hypertension can lead to diseases that affect the heart, the brain or the vascular system. The data from the Framingham Heart Study demonstrates that sustained hypertension increases the risk of myocardial infarction which can result in disability or death [272]. High blood pressure due to hypertension can often affect and damage specific organs. This phenomenon, called "Target Organ Damage" can lead to diseases of specific organ systems such as the heart, brain, kidney or retina:

Heart and blood vessels : Hypertension has been known to cause coronary artery disease, and left ventricular hypertrophy which may lead to subsequent heart failure. Hypertension has been known to be a factor which can acclerate atherosclerosis [101], a condition where plaque builds up inside the arteries. When atherosclerosis affects the coronary artery it is called coronary artery disease (also called coronary heart disease) which is one of the leading causes of death in the modern world. Hypertension can also cause left ventricular hypertrophy which is the enlargement, thickening (hypertrophy) and weakening of the walls of the left ventricle. If not treated in time, the end result of most of these conditions which affect the heart and the blood vessels is subsequent heart failure.

Brain : Studies have shown that hypertensive target organ damage of the brain is associated with cognitive impairment and decline in memory [55]. Hypertension and high blood pressure in early or early or mid-life increases the chances of brain atrophy in later life [146]. A recent study [261] demonstrated that the increase of the signs of target organ damage due to hypertension is correlated with decrease in the memory functions of the brain. The Framingham Heart Study demonstrated that untreated hypertension leads to decrease in cognitive performance, attention and memory [87, 88]. One of the most common causes of death due to hypertension is stroke or cerebrovascular accident (CVA) where decrease in blood flow to the cells of the brain can lead to cell death.

Kidney : Hypertension also affects the renal system and is one of the major causes for the development of chronic kidney disease which damaged the blood vessels in the kidneys. Chronic kidney disease can lead to the build up of fluid and waste products in the body which in turn affects the normal bodily functions. Controlling blood pressure has been shown to slow down kidney damage. Unless controlled, chronic kidney disease can progress to end-stage renal disease (also known as renal failure).

Eyes : Hypertensive retinopathy is a condition where high blood pressure causes changes in the retina leading to the narrowing of the retinal arterioles. This might lead to headaches, double or reduced vision.

If hypertension is treated at an early stage and blood pressure is lowered, it may stop the progression of the diseases of the target organs. In some cases the lowering of blood pressure, if done early enough, can reverse the target organ damage to a certain extent. This highlights the urgent need for early detection and treatment of hypertension.

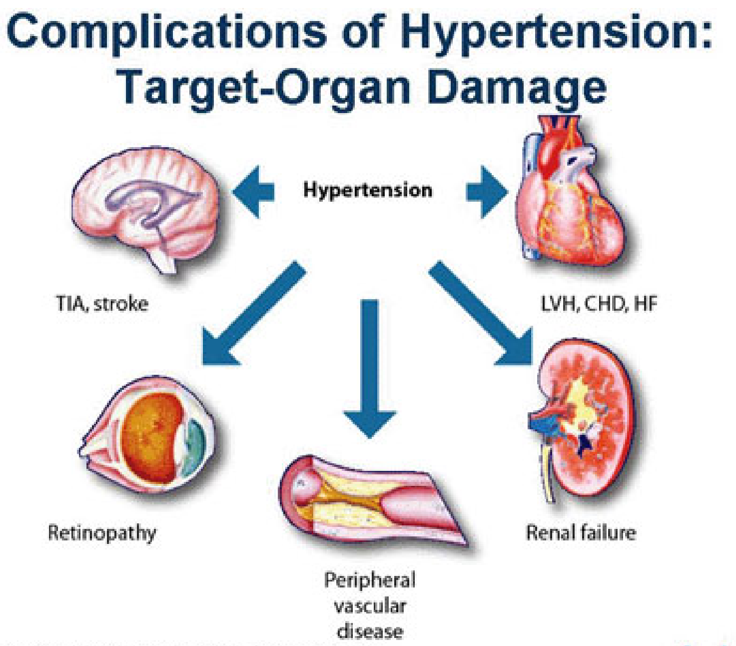


Figure 3.2: Complications arising out of hypertension which can cause target organ damage.

3.2 Diagnosis of Hypertension

According to the clinical practice guidelines published jointly by the American Society of Hypertension and the International Society of Hypertension [266], individuals are classified into their blood pressure stages on the basis of their systolic and diastolic blood pressures (SBP and DBP) as shown in table 3.1. When there is a disparity between the SBP and DBP, then the patient is classified into the higher stage [257].

Blood Pressure Stage	Blood Pressure Range
Normal	SBP <120 and DBP <80 mm Hg
Prehypertension	SBP 120 - 139 or DBP 80-89 mm Hg
Stage 1 Hypertension	SBP 140 - 159 or DBP 90-99 mm Hg
Stage 2 Hypertension	SBP >= or DBP >= 100 mm Hg

Table 3.1: The clinical practice guideline for the classification of hypertension.

The most common method of diagnosis of hypertension is the detection of high-blood pressure using a brachial cuff-based measurement device or an automated electronic measurement device. The guidelines for diagnosis of hypertension [266] jointly written by the American Society of Hypertension and the International Society of Hypertension specify a strict protocol for measurement of blood-pressure under clinical settings. It states, among other rules, that blood pressure should be measured in both arms and the higher reading should be used for diagnosis. It recommends that at least two readings, 1-2 minutes apart be taken, and the average be used. It also states that standing blood pressure using the same protocol be recorded to account for differences in posture. Even if all the guidelines are followed to the letter, there are other factors which can affect the diagnosis of hypertension. Conditions such as “white-coat hypertension" and “masked hypertension" can often lead to misdiagnosis. White-coat hypertension is defined as elevated blood pressure (BP $\geq$ 140/90 mmHg) under clinical settings but normal otherwise. Masked hypertension is defined as a normal blood pressure (BP) in the clinic or office ($\leq$ 140/90 mmHg), but an elevated BP out of the clinic (ambulatory daytime BP or home BP $\leq$ 135/85 mmHg). Even for patients not suffering from such conditions, accurate recording of blood pressure is not an easy task. Blood pressure is affected by the time of the day, the stress level of the patient, and factors such as whether the patient has recently smoked or drank coffee. Owing to all these factors, it has been argued that a limited number of measurements within a short period of time may not be enough for the accurate diagnosis of hypertension under clinical settings, and repeated monitoring is the only safe and sure way of diagnosis of hypertension.

Ayaman and Goldshine [29] in 1940 demonstrated the effectiveness of home based blood pressure monitoring for the accurate diagnosis of hypertension. They identified that home blood pressure could be 30 to 40 mm Hg lower than that measured by the physician under clinical settings. Home-based self monitoring has the practical advantage of eliminating the white-coat effect and also allows for monitoring the patient’s response to anti-hypertensive treatment. While doctors have advocated the use of ambulatory blood pressure measuring devices for continuous monitoring, they are usually adopted by patients who are already hypertensive or have been diagnosed with a high risk of hypertension. It is not very common for healthy people to regularly monitor their blood pressure.

One main issue with large scale adoption is that regular measurement is not easy. Even for those suffering from hypertension the patient or patient-families have to bear the burden of regular measurement. The complexity of use and calibration of blood-pressure measurement devices by the patients makes this frequent measurement cumbersome. There is a need to develop techniques for continuously and unobtrusively monitor the status of hypertension among people.

3.2.1 Physiological Markers for Hypertension

While presence of elevated blood pressure is used as the most common definition of hypertension, a recent (2009) paper [110] published by the American Society of Hypertension in the Journal of Clinical Hypertension defines hypertension as a *"progressive cardiovascular syndrome arising from complex and interrelated etiologies"*. It states that progression of hypertension is strongly associated with functional and structural changes to the cardiac and vascular system, and early markers of these changes are often present before elevated blood pressure is detected. Due to this, the authors concludes that *"hypertension cannot be classified solely by discrete blood pressure thresholds."*

Studies have demonstrated that continuous increase in the activity of the sympathetic nervous system is indicative of health problems. Our sympathetic nervous system controls our "fight or flight" response[145]. Increase in the activity of the sympathetic nervous system is a major determinant of elevated blood pressure. Sympathetic over-activation leads to stimulation of the heart and the peripheral vascular system. This leads to increased cardiac output. Since blood pressure is a product of cardiac output, elevation of heart rate also leads to elevation of blood pressure. Measurement of Heart Rate Variability (HRV) has thus been shown to be an effective measure for the detection and prediction of hypertension [94]. Studies [179, 231] have demonstrated that the sympathetic activation is an important indicator for early diagnosis of hypertension. Population studies such as the Coronary Artery Risk Development in Young Adults

(CARDIA) study [102], have shown a positive correlation between heart rate and the development of hypertension.

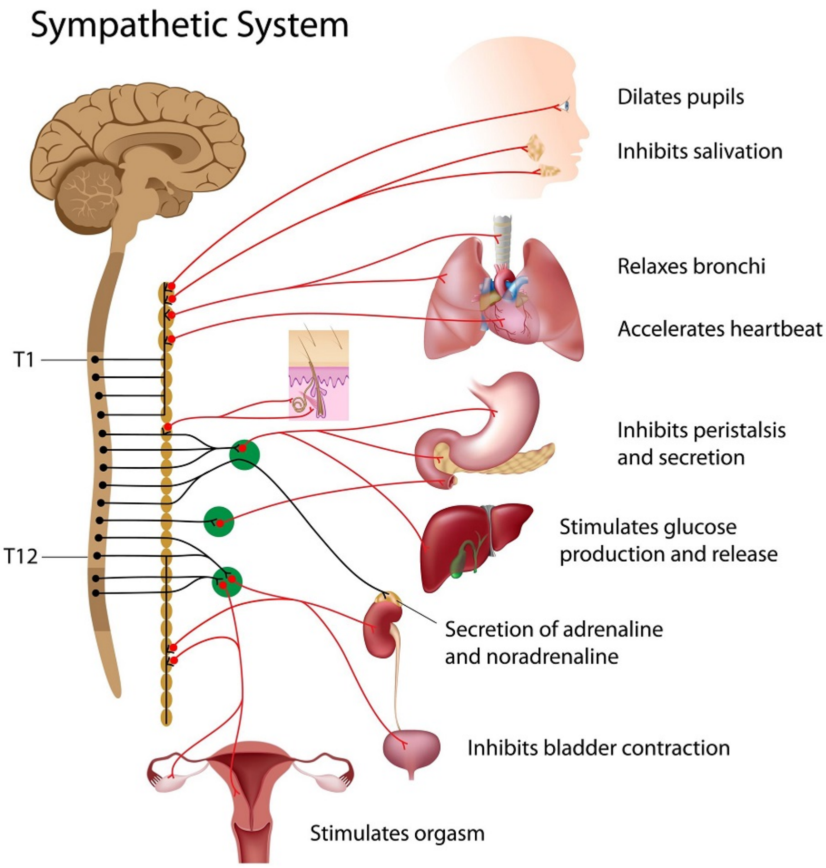


Figure 3.3: Sympathetic activation affects the peripheral nervous system and leads to changes in heart rate, skin temperature and electrodermal activity (EDA) among others.

This sympathetic activation also affects the peripheral nervous system causing changes in other physiological signals such as skin temperature and electrodermal activity (EDA) [251]. Variations in these physiological signals can thus be indicative of sympathetic activation, and have long been studied for research into the analysis of the stress response of the human body [52, 130, 30]. In this research we hypothesize that tracking and measuring the variations of these physiological signals (electrodermal activity, skin temperature, heart rate) also hold potential for the detection and monitoring of hypertension. A big motivation behind using physiological signals such as skin temperature, heart rate and electrodermal activity in hypertension research is that, unlike blood pressure monitors, there exist wearable, lightweight and unobtrusive devices for the measurement of these signals. In recent years there has been an increase in the adoption of wearable devices such as Empatica E3 and E4 [3], Microsoft Band [13] and Basis Armband [14]. Using these devices for tracking and monitoring physiological signals has opened up an opportunity for early detection and intervention for hypertension. In the following chapters we demonstrate the use of wearable device for continuous monitoring of these physiological signals and how they can be used to detect stress and hypertension. We show that combinations of heart rate, electrodermal activity and skin temperature signals can be successfully used for the detection of hypertension.

3.3 Factors Affecting Physiological Signals

Continuous monitoring of physiological signals is not without its challenges. Physiological signals (blood pressure, heart rate, electrodermal activity and skin temperature) are affected by a number of internal and external factors and show considerable variations throughout the day. They are affected by the environmental factors such as temperature and humidity, and our current context such as activity level.

Consumption of caffeine, alcohol and nicotine are known to affect these physiological signals. Alcohol consumption can decrease heart rate [221] while caffeine increases it [274]. Cigarette smoking increases sympathetic outflow which raises both heart rate and blood pressure [199]. Physical activities such as walking, running, and exercise raise the values of all physiological signals. Emotional Stress can produce marked increase in heart rate, blood pressure and electrodermal activity. Even talking or reading aloud raises both heart rate and blood pressure.

There is a need to determine these contextual factors while employing ambulatory monitoring of physiological signals. In controlled experimental scenarios this monitoring can be done by a third party observer who can note down the user's context. In case of home-based monitoring of blood pressure, doctors advise patients to self-report the conditions to note down their current or recent activity and state in the form of a diary. However, in on-the-go scenarios, a paper based diary is not an effective and usable solution and a continuous digital tracking system is necessary to simplify the note-taking and context detection.

We demonstrate the use of a intelligent personal mobile agent which can simplify the annotation and note-taking process for the patients through a multi-modal note-taking approach using both text and voice. This personal mobile agent can also continuously and automatically detect the activity of the user. These details can contextualize the changes in the physiological signals and can help to identify the factors that affect these signals in real-world on-the-go scenarios.

3.4 Management of Hypertension

Management of Hypertension consists of both pharmacological and non-pharmacological approaches. Pharmacological interventions are necessary for patients at a later stage of hypertension. However, for patients with pre-hypertension or mild primary hypertension, a non-pharmacological approach through lifestyle modification can help keep blood pressure under control. Even for patients taking drugs for hypertension, non pharmacological methods have been shown to provide further health benefits.

3.4.1 Non-Pharmacological Approach Towards Hypertension Management

Lifestyle modification has been shown to be beneficial for patients suffering from hypertension. Following a healthy diet and increasing exercise regimens have been shown to be effective non-pharmacological factors for decreasing blood pressure as well as reducing the risk of cardiovascular diseases. The following factors have been shown to be effective non-pharmacological interventions for hypertension management:

Decreasing obersity: Obesity, specifically visceral obesity, is an important risk factor for hypertension and cardiovascular disease [242]. A recent research discovered that the hormone leptin which is secreted by the adipose tissue is significantly elevated following weight gain. The original function of Leptin is a) to decreases appetite, and b) increase energy expenditure through sympathetic activation. It has been shown that during obesity the body develops resistance to the appetite-decreasing effect of leptin. However, it still contributes to the sympathetic activation of the nervous system, thus increasing blood pressure. Because of this, weight-loss is one of the key non-pharmacological advice given to hypertensive patients.

Diet and Salt Reduction: Proper diet can thus be a very important factor in controlling hypertension. The Dietary Approaches to Stop Hypertension (DASH) [223] confirmed that a healthy diet can benefit people suffering from hypertension. It demonstrated that an alteration in diet with increased fruits, vegetables, and low-fat dairy products and decreased amounts of total and saturated fat and cholesterol is beneficial in lowering blood pressure.

Primary hypertension is more common in populations with a high intake of sodium. It has been shown that hypertension is mostly absent in populations consuming less than 3 grams of sodium per day, and is highly prevalent in populations consuming more than 20 grams per day [191]. A reduction of salt intake can lead to decrease in both systolic and diastolic blood pressure in hypertensive as well as normotensive subjects. The World Health Organization recommends that the daily intake of salt should not be more than 5 grams per day [129].

Exercise: A long term, regular exercise regimen has been shown to decrease blood pressure [118, 92]. Although blood pressure and heart rate temporarily increases during exercise, it rapidly returns to normal levels after the completion of exercise. There is even an acute fall in blood pressure after an exercise session, and this is called a *post-exercise hypotension* [119]. Researchers have suggested that this phenonomenon of post-exercise hypotension can be exploited as a non-pharmacological and practical intervention for the management of hypertension [174]. A 16-week study performed on 56 patients suffering from hypertension [80] demonstrated that regular exercise led to a significant reduction of both systolic and diastolic blood pressure compared with controls.

Decrease in Alcohol consumption: Although several studies have shown that moderate alcohol consumption (especially red wine) is beneficial for the heart, research also points out that regular over-consumption of alcohol can increase blood pressure [212]. There is evidence to show that this is a reversible process and cessation of alcohol consumption by hypertensive patients who are heavy drinkers lowers blood pressure [177].

Smoking cessation: Smoking is one of the major risk factors for cardiovascular disease. The INTERHEART study [275] which investigated the risk factors associated with myocardial infarction demonstrated that even smoking between 1 to 5 cigarettes daily increases the risk of acute myocardial infarction by 40%. Smoking increases myocardial oxygen consumption and leads to rise in both heart rate and blood pressure. Thus a reduction or complete quitting of smoking can be effective for control of hypertension and improvement of overall cardiovascular health.

Non-pharmacological approaches are hard to implement because it is difficult to track them and motivate people to comply with them. There is a need for developing technologies which can make these non-pharmacological management techniques easier by increasing the agency of the patients. In the following chapters we describe how a intelligent personal mobile agent can elicit annotations, and also track stress and activity levels to engage patients in their own care.

3.4.2 Models of Hypertension Management

The standard care model consists of patients visiting their physicians on a regular basis for diagnosis and tracking of symptoms (eg. blood pressure). However, there are there are two major problems with this standard care model:

a) Limited time with each patient: A Physician can spend a very limited amount of time with a patient. This short time may not be adequate to identify and treat all the multiple complex problems underlying a disease. In the case of hypertension, which is a condition related to lifestyle, there may be several personal and social factors which can affect diagnosis and care management. It may be difficult for a physician to glean all the information and understand all the underlying causes during a patient's visit.

b) Difficulty in enforcing adherence: Once a patient leaves the clinic, there is very little a physician can do to ensure that the patient is compliant with the provided advice. Ascertaining that the patient is adhering to the treatment protocol is often done by simply asking the patient. Once the patient has left the clinic, it is difficult for the physician to enforce adherence to the treatment regime.

Due to this, care providers are trying out new care models. Two popular care models which can complement the physician led care model are **self-management** and **team-based care management**. We discuss both these models below, and suggest a third model for hypertension management involving an intelligent personal agent.

Self-management of Hypertension

Self-management of hypertension primarily involves keeping track of the disease condition through regular home-based blood pressure monitoring. While paper and diary based monitoring methods have been used traditionally, in recent times mobile technologies have been used to promote self-management among hypertensive patients. Studies have shown that home-based blood pressure monitoring can provide improvement in blood pressure control among hypertensive patients. The THOP trial [247] showed that home based blood pressure monitoring is more beneficial than conventional measurement of blood pressure at a doctor's office. In this trial 25.6% of the patients in the home-based BPM group were able to achieve recommended blood pressure levels compared to only 11.3% patients in the office BP measurement group.

The TASHMIN2 Trial [189] demonstrated the effectiveness of self-management of hypertension. It included 536 patients with elevated BP levels ($>$ 140/90 mm Hg) who were split into self-management (n=263) and usual care (n=246). The group using self-monitoring also used self-titration of antihypertensive drugs according to a predefined plan. Over a six month period the self-management group observed greater reductions in mean systolic blood pressure compared to the usual care group (difference between groups 3.7 mm Hg). Over a one-year period, the reduction in systolic BP was 5.4 mm Hg greater in the intervention group than in the control (usual care) group.

However, one major concern with self management of hypertension is that for certain patients self-measurement of blood pressure can induce an added anxiety. For patients who might become obsessed with their blood pressure reading, self-monitoring can be counter-productive and even lead to an increase in the blood pressure.

Team-based Care Management of Hypertension

The team based care model [44] goes a step ahead of the self-management model. It aims to improve the primary care of chronic illnesses by increasing the number of participants involved in the care of a patient. It suggests that the physician-patient model should evolve into a wholesome care delivery plan which involves getting the entire community (including the health care organization, local community, clinical information systems and the patient himself) included in the care. The team-based care model suggests that a care team consisting of non-physician members should follow the patient to assist in care-management. This care team could include pharmacists, nurses, social workers, and other members depending on the needs of each individual patient. These members of the care team can provide different levels of support to the patient when he or she is not with the physician. A recent meta review [63] of clinical trials in the United States found that including pharmacists in providing care to the patient showed statistically significant improvement in blood pressure, cholesterol, and medical adherence among patients. In another study, Lindsay et al [171] applied a a team based care bundle to the chronic care model for blood pressure management among diabetic patients across 4 sites in the United States of America. Results showed a statistically significant decrease in the proportion of patients with uncontrolled blood pressure in 3 out of the 4 sites, and a statistically significant improvement in the satisfaction survey among the patients.

3.4.3 Intelligent Personal Agent Based Care Management for Hypertension

While the Team-based Care Model is more successful than simple self-management with home-based blood pressure monitoring, implementing it requires a complex team-based effort. Getting a community of players involved in patient-care introduces complexities in large scale implementation. There is a need for simplification of the care by bridging the gap between self-management and the team-based care model and automating some aspects of the latter.

Technology assisted models such as mobile health (mHealth) involves the use of technologies such as mobile phones and connected devices for simplifying care management of patients suffering from chronic diseases. mHealth empowers the patient by providing new ways to improve home-based self-monitoring. In a connected health scenario, monitoring devices can be automatically connected to mobile phone networks to ease the burden of measurement and record keeping. Mobile applications can help in taking notes and tracking symptoms. This data can automatically be transmitted to the doctors, thus avoiding careful physical maintenance of the notes by the patient. Automatic reminders for medication can help in improving adherence and management while avoiding the cost and complexity of a human team-based effort required in the chronic-care model.

However, mobile health technologies, by themselves are not intelligent. They only improve connectivity among the various participants in the healthcare scenario. Ambulatory monitoring, as mentioned before, needs to identify and understand the context of the user. It also needs to analyse the collected data and extract useful knowledge from it to make it actionable. While in the team-based care model, this can be done by the care team, in a self-management model this is challenging. Understanding the user's behaviour including activity level and stress of the user is even more difficult. Continuous annotation of stress and activity levels can be a tedious process for a user. There is a need for automatic detection of these metrics.

This is where we propose the use of an intelligent personal agent-based care management plan where the intelligent agent replaces most of the tasks done by the chronic care team. An intelligent agent can help the patient in recording and maintaining notes. It can automatically seek annotations when required, monitor the activity level, and learn to detect the stress level of the user. Using wearable devices which can record the physiological signals such as heart rate, electrodermal activity, and skin temperature, the intelligent agent can identify the level of stress of the patient. Using the motion sensors on the patient's mobile phone the intelligent agent can detect the activity level of the user. Using this data, the intelligent agent can build up a personal model which accurately represents the user. Use of an intelligent personal agent need not be restricted to patients who have been diagnosed with hypertension (or other chronic diseases) - its use by healthy individuals can help in better lifestyle management by increasing their awareness about their stress and activity levels. Such an agent can also detect the early signals for hypertension and help prevent the occurrence of the disease. In the following chapters we present the intelligent agent platform and discuss about its application in the various aspects of health care management.

3.5 Conclusion

Hypertension is a complex disease which can be difficult to track and manage. In this chapter we explore the traditional methods of diagnosis and management of hypertension. We also discuss how physiological markers such as heart rate variability and electrodermal activity are affected by the condition of hypertension. We propose the use of these signals for the detection of hypertension. We also explore the various approaches for management of hypertension, and propose a novel model of using an intelligent personal agent for the management of the disease.

4

The Health Analytics (HEAL) Platform

"A doctor who cannot take a good history and a patient who cannot give one are in danger of giving and receiving bad treatment."

– Paul Dudley White , *Clues in the Diagnosis and Treatment of Heart Disease (1956)*

Knowledge of the complete clinical history, lifestyle, behaviour, medication adherence data, and underlying symptoms all affect treatment outcomes. Collecting, analyzing and using all this data while treating a patient can often be very challenging. A doctor can spend only a limited time with a patient. This time is often not enough to learn about all the lifestyle and underlying conditions of a patient's life. The data reported by a patient also suffers from bias in memory. A doctor might advise a patient to walk more, eat healthier, and decrease their stress level, but once a patient is out of the clinic, it is very difficult to ensure that the patient actually follows all these directives. Often patients are asked to maintain diaries of their daily activities. Diaries can help to improve adherence by increasing the conciousness of the patients, and can also serve as a way for the doctors to validate this adherence. However, diaries can be cumbersome to parse, and hence increases the task of the doctor.

The role of an intermediary care team which can follow the patient [190] and ensure adherence and protocol has been suggested as a solution. However, setting up a care-team is complex and expensive. There is a need for a technological solution which can monitor and assist patients in their daily lives and ensure that the doctor receives a clear picture of the patient's lifestyle.

The recent growth in the sensing and processing power of smartphones have turned them into ubiquitous computing devices. They are always there with the users and have become an emerging platform for social, behavioural and environmental data science. Smartphones have become a time and cost effective platform for research in social [214], health [175], behavioural [77], and clinical [206, 93] sciences. Smartphones, in conjunction with wearable devices can provide a complete long-term understanding of the user's physical, environmental, and behavioural patterns. They have been successfully applied for detecting and tracking and managing complex symptoms such as diabetes [156], depression [42], bipolar disorder [213], and pulmonary diseases [180] . Smartphones have also been shown to be highly effective in improving medical adherence [75] and patient empowerment in chronic diseases [252].

4.1 Motivation and Goals

Effectively caring for patients suffering from chronic diseases is a challenging task. There is a need of decreasing the burden of the primary care physician in treating chronic patients, while increasing the quality of the care provided to the patient. This requires adoption of new policies as well as technological methodologies.

Mobile health platforms which automate some parts of the care management process have shown to lower costs while increasing patient engagement. Mobile health has been shown to work effectively in medical adherence, as well as disease condition management. One criticism of mobile health platforms are that they are only recommendation or data collection tools and most of them lack the capability of understanding the patient's context. They are also not personalized and lack the ability to adapt according to the state of the user (patient). Because of this, clinical intervention which includes a human caregiver (human in the loop) to follow the patient has been shown to be more effective than mobile health alone.

In this work we wanted to address this challenge of understanding the user's state to personalize care-management. A mobile personal agent capable of tracking and understanding a patient can greatly improve and personalize chronic care management. We apply our agent technology to patients suffering from essential hypertension and show that a intelligent personal mobile agent is capable of monitoring, analyzing and tracking several characteristics of hypertension management. Patient reports also show improved patient satisfaction with using a personal mobile agent.

4.2 Platform Overview

The Health Analytics (HEAL) Intelligent Agent platform 4.1 consists of three components:

- ***Empatica wristband:*** The Empatica E3[1] wristband is a bluetooth enabled wearable device capable of sensing physiological signals. It is an unobtrusive, wearable, lightweight, wireless, multi-sensory signal acquisition device which is worn on the wrist like a watch. Its small form factor makes it ideal for ambulatory recording of physiological

[1] www.empatica.com

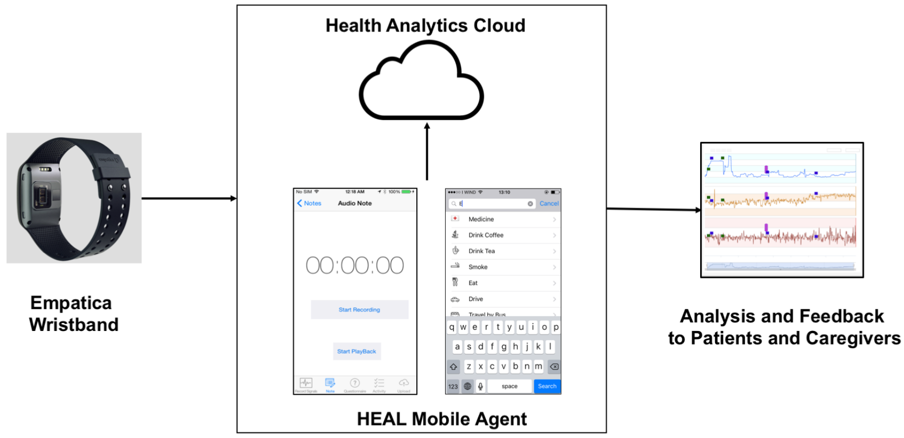


Figure 4.1: The three components of the HEAL platform. The Empatica E3 wristband, the HEAL intelligent agent, and the HEAL cloud

signals in the wild, with possible applications in research and health care domains. It has four inbuilt sensors which are capable of measuring and reporting a) Electrodermal Activity (EDA), b) Blood Volume Pulse (BVP), c) Inter Beat Interval (IBI), and d) Tri-Axial Acceleration.

- ***HEAL intelligent agent:*** The HEAL intelligent personal agent is a custom designed companion application which resides on the user's iPhone. The HEAL mobile companion runs on any iOS device which supports the bluetooth low energy (BLE) protocol (iPhone 4s and up). It is a personal companion application which records and securely uploads the physiological signals from the Empatica E3 wristband to the server. The personal companion also acts as an agent to elicit information from the user through questionnaires and text and speech.

- ***The HEAL cloud*** - The Health Analytics (HEAL) cloud is the server component of the HEAL Intelligent Agent platform. All the individual HEAL mobile companions upload their data to the HEAL cloud. The HEAL cloud encrypts and stores the data for secure access. At the back-end, the HEAL cloud stores, parses, structures, cleans and runs machine learning algorithms on the data to learn about the user's behaviour including the user's activity and stress levels. The cloud also provides a web visualization platform which can be accessed by the patient as a lifelogging tool, and also by the doctors for keeping track of their patients.

4.3 The Empatica E3 wristband

The Empatica E3 (Figure 4.2) has four integrated sensors a) an electrodermal activity (EDA) sensor b) a photoplethysmography (PPG) sensors c) a temperature sensor d) a tri-axial accelerometer. When active, it continuously records signals from these sensors. It and can connect to a bluetooth enabled smartphone (Android or iOS) over the bluetooth low energy (BLE) protocol to stream the recorded data to a companion application on the phone. On a single charge the E3 device lasts for about 10 to 12 hours in streaming mode, making it ideal for ambulatory data collection during a typical workday.

Figure 4.2: Empatica E3 wristband - wearable, lightweight, wireless, multi-sensory data acquisition device

4.3.1 Recorded Signals

The sensors on the Empatica E3 record the following signals at the following sampling rates:

- Blood Volume Pulse (BVP): The E3 reports BVP at a 64 Hz rate.
- Electrodermal Activity (EDA): EDA is reported at a 4 Hz rate.
- Inter Beat Interval (IBI): IBI is reported as a time-IBI pair.
- Skin Temperature: Skin Temperature is reported at a 2 Hz rate.
- Tri-Axial Acceleration: XYZ Acceleration of the wristband is reported at a 32 Hz rate.

4.4 The HEAL Intelligent Agent

The HEAL intelligent agent runs on any iOS device supports the bluetooth low energy (BLE) protocol (iPhone 4s and up). The HEAL intelligent agent has four main functions:

- It connects to the Empatica E3 device to continuously record and upload the streaming physiological signals from the wristband.
- The agent also records the data from the sensors on the smartphone.
- The agent transmits the data for analysis on the HEAL cloud.
- The agent elicits information from the user using multiple strategies including predefined questionnaires, list-based activity annotations, and free open text and voice notes.

4.4.1 Signal Storing and Streaming

The HEAL intelligent agent connects to the E3 device and continuously stores all the physiological signals in a time, value pair format. The HEAL intelligent agent uploads the data to the cloud in two steps:

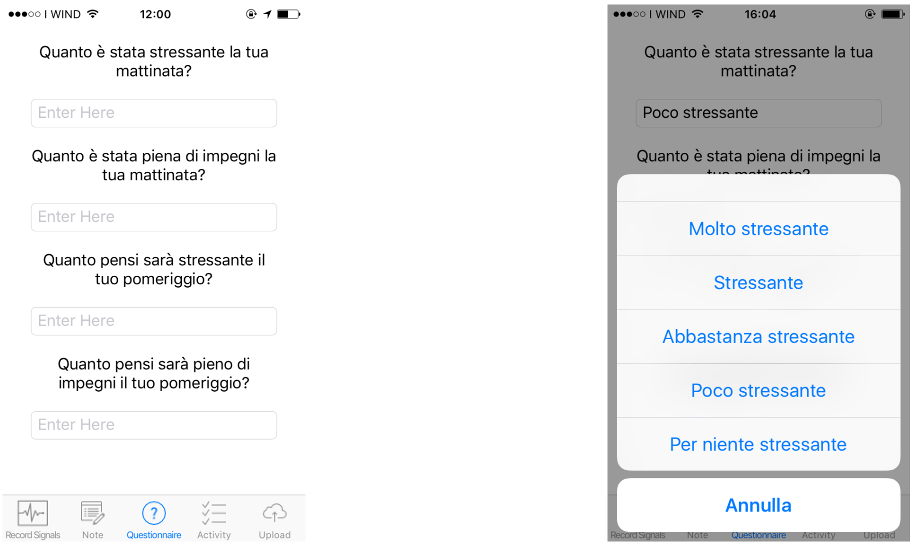
(a) Streaming mode: Whenever the HEAL intelligent agent is actively collecting data, it continuously streams a down-sampled version of the data to the HEAL cloud. This downsampled data is used for live visualization of the physiological and activity signals. This data is streamed once every minute. The data is uploaded in a json format.

(b) Bulk mode: At the end of the day, the user can upload the entire signal stream to the HEAL cloud. This upload is also triggered automatically if the HEAL agent detects that the user has not manually uploaded the data for some time (2 days) and the iPhone is connected over a wifi-network (Due to restrictions on the iOS platform, this automatic upload can only occur when the iPhone is also connected to the empatica device - otherwise background uploads on the iOS have a timeout). Since the data for two days can be quite large, this upload is done over the wifi-network to decrease the mobile data consumption by the application while ensuring that the data is uploaded to the analytics platform. At the time of the upload, the data for each session is compressed and a MD5 (Message-Digest algorithm 5) checksum for the file is calculated. The compressed file along with its checksum is uploaded to the server.

4.4.2 Overt Signal Acquisition

The HEAL platform uses both interval-contingent and event-contingent recording strategies. In interval-contingent recording, data are collected at regular intervals determined, i.e. once every three hours (when the user wears the device, after three hours, and at the end of the daily data collection). In event-contingent reporting, users can record a report every time he or she appreciates that an stressful event has occurred. Using these strategies the HEAL platform collects the following overt signals:

1. Periodic Structured Information in the form of **anticipated and perceived stress and workload questionnaire**
2. Spontaneous Structured Information in the form of **event annotations**
3. Spontaneous Structured Information in the form of **user diaries**



(a) Stress Workload Questionnaire (b) Reporting the Stress Level

Figure 4.3: The HEAL Companion for recording anticipated and reported stress and workload

Anticipated and Perceived Stress and Workload Questionnaire

The HEAL intelligent agent uses interval-contingent strategies to periodically record information about a user's stress and workload level (Fig. 4.3).

Anticipated Stress and Workload Reporting : This is a user report of the level of stress and workload for the upcoming period.
Perceived Stress and Workload Reporting : This is a user report the level of stress and workload perceived for the period which has passed.

At the beginning of the day the user is asked to record the **anticipated stress** and **anticipated workload** levels for their morning session.

(a) The Stress annotations are obtained on a five point likert scale as follows:

- Not at all stressful (per niente stressante)
- Little stressful (poco stressante)
- Moderately Stressful (abbastanza stressante)
- Quite stressful (stressante)

- Very Stressful(molto stressante)

(b) The Workload annotations are also obtained on a similar five point likert scale:

- Not at all busy (per niente piena)
- Little busy (poco piena)
- Moderately busy (abbastanza piena)
- Quite busy (piena)
- Very busy(molto piena)

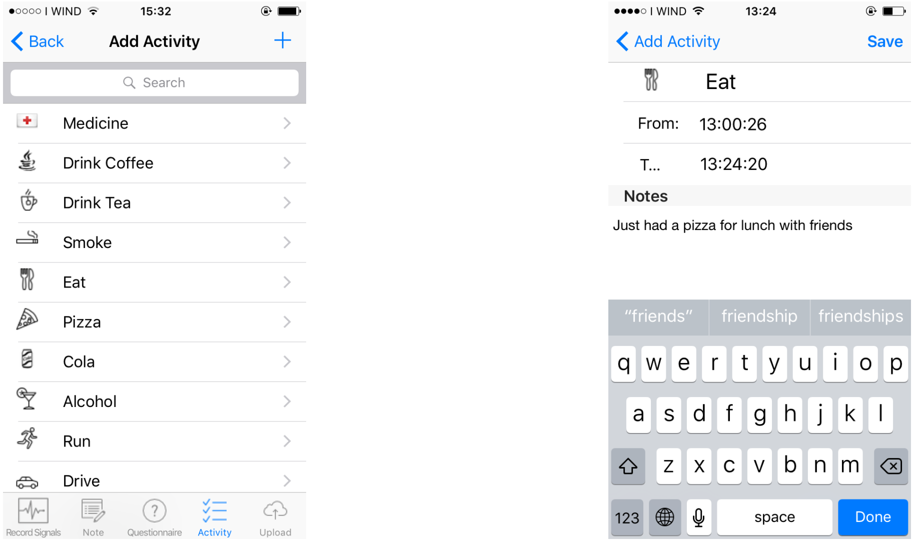
Around noon, the users are asked the same question as above, but this time they are required to assess how their morning really was, and provide their prediction for the afternoon. At the end of the afternoon they will be asked to assess how stressful and busy their afternoon really was.

Event Annotations

The HEAL intelligent agent encourages the user to annotate events and activities during the day. These annotations can provide a deeper understanding of the user's activity level and habits. These annotations are also used later to ground the automatic activity recognition done on the analytic cloud. Analysis of these activities can also be used to identify the stress inducing activities in a user's everyday life.

User Diaries

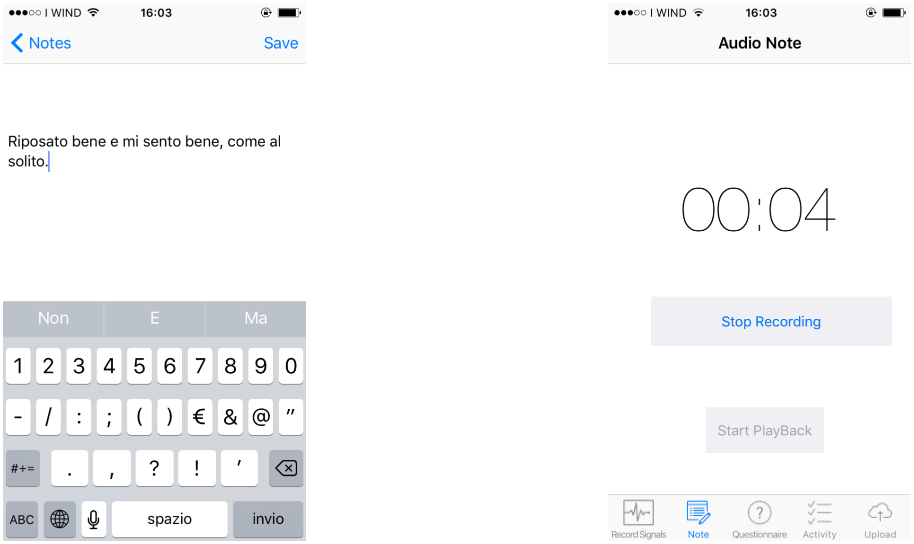
Our experiences are inherently temporal in nature. After some time we tend to forget the exact nature of the event and the emotions it invoked at the time. Diaries are self-reports to capture daily events, interactions, mood and reflections. Diaries are a popular tool for life-logging for memory aiding and recollection [150]. The reflective nature of the process of writing and reading one's own diary has been shown to increase self-awareness



(a) Add a new activity

(b) today's activites

Figure 4.4: The HEAL intelligent agent application allows the user to add and annotate activities throughout the day.



(a) text notes

(b) audio notes

Figure 4.5: The HEAL intelligent agent application for diary keeping - the user can either write down text about his feelings and situations, or narrate it using speech.

about physical activity or emotional states in different situations.

Diaries have been shown to be very effective in gaining a deep insight into a patient's well-being and can be used by a therapist for learning about the patient's behaviour and routines. They can also be used for tracking medicine adherence and compliance to treatment regimes. In psychology research diaries have been shown to be an effective tool in promoting psychological recovery for patients suffering from various symptoms like anxiety, depression, and post-traumatic stress [22].

One of the main challenges of diary-keeping is the need to carry around the physical diary, and finding the right place and time to record one's thoughts. The growth of mobile phones in our lives has resolved this problem - it provides an easy interface to write or speak to. The HEAL mobile companion encourages the user to maintain a multimodal diary (Figure 4.5) - the user can either take frequent notes or record speech about his or her feelings, current state, and elicit about the surroundings, and how his day is.

4.5 The Health Analytics cloud

The analysis and machine learning for the intelligent agent is performed on the Health Analytics (HEAL) cloud. The HEAL cloud has three parts - (1) Data Processing Engine (2) Analytic Engine (3) Visualization Dashboard (see Figure 4.6).

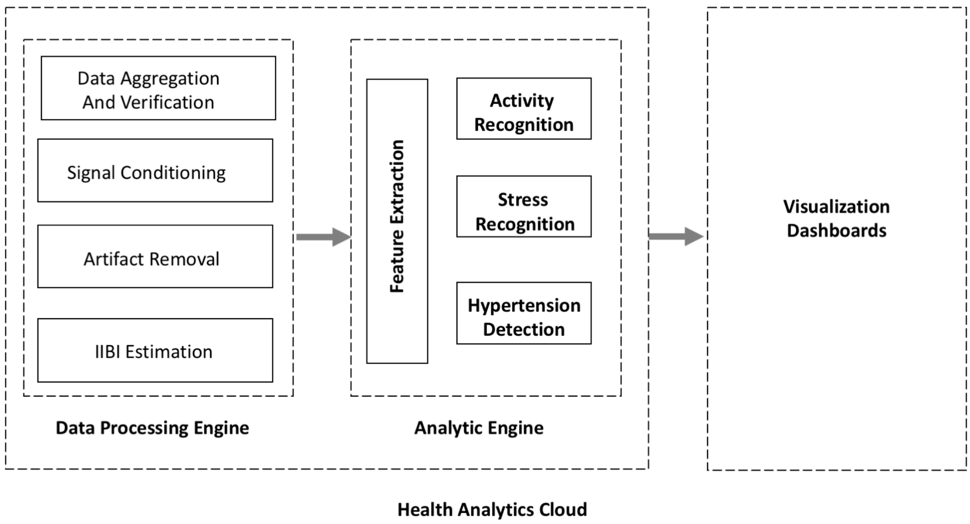


Figure 4.6: The Health Analytics Cloud Pipeline. The pipeline consists of the (1) Data Processing Engine (2) Analytic Engine (3) Visualization Dashboard

4.5.1 Data Processing Engine

The data preprocessing engine performs the various subtasks involved in preparing the data and signals for feature extraction and machine learning performed by the analytic engine. It consists of four components:

(a) Data aggregation and verification : The data from the intelligent agent application is uploaded to the Health Analytics cloud. The backend uses a mysql database to store all the structured data. The database uses row level encryption for sensitive user profile data. The signals and the audio themselves are stored on the disk, and their references are saved to the database table.The json files from the streaming data are parsed and entered into the mysql database for continuous visualization through the HEAL dashboard. For the end of the day data, the compressed files are decompressed and their validity is checked against their md5 checksum. In case a problem is detected a message is returned to the HEAL application to re-compress and upload the file which doesn't match the checksum. The same step is taken for the audio files uploaded from the HEAL intelligent agent.

(b) Signal Conditioning: The signal conditioning module is responsible for signal processing. The electrodermal activity (EDA) and skin temperature signals are passed through a low pass filter and detrended. The accelerometer signal is used for active noise cancellation from the blood volume pulse (BVP) signal (as described in [109]) which is used in the inter-beat-interval (IBI) estimation module. Based on the specific application (activity recognition, stress detection and hypertension detection), different signal processing techniques are applied in the HEAL Data Processing Engine. The individual signal processing techniques will be discussed in their respective chapters.

(c) Artifact Removal: Physiological signals are highly susceptible to artifacts which can limit their usage for identification of the mental state of the user. Removing artifacts is therefore a very important and essential part of the activity and recognition pipeline. The HEAL analytic engine identifies and removes artifacts such as local noise, artifacts due to pressure, nervous fidgeting and gross body movements. This process is explained in Section 7.6.3.

(d) IIBI Estimation: This module estimates the interpolated inter-beat-interval signal from the conditioned blood volume pulse (BVP) signal. This process is explained in Section 8.6.1.

4.5.2 Analytic Engine

The analytic engine consists of the following modules:

(a) Feature extraction: The feature extraction module extracts various features from the physiological, motion, and user profile data.

(b) Activity recognition: The activity recognition module performs activity recognition explained in Chapter 6, to identify the current activity of the user. The activities recognized include walking, standing, sitting, travelling by bus, travelling by car/driving, and travelling my train.

(c) Stress recognition: The stress recognition module performs stress recognition using the physiological signals of the user. The stress process is explained in Chapter 7.

(d) Hypertension detection: Using all the data above (including the stress and activity data), the analytic engine can distinguish between normotensive and hypetensive users. This can help in early detection of hypertension. This work is explained in detail in Chapter 8.

4.5.3 Visualization Dashboard

The HEAL Dashboard acts as a visualization, annotation and analysis platform for the users/patients and the care team. The dashboard visualizes the streaming physiological signal data and adds context to it by adding the patient supplied notes, and the annotations on the signal timeline. The patients have their individual login and can view their own data, and at the end of the day edit, delete or add their data. This can be used as a reflective tool by the patient to perceive their physiological response to the various stressors in their life (Figure 4.7).

The healthcare team has access to the data to keep track of the most important vital signs of the patients during the day (Figure 4.7). In the streaming mode, they can see minute by minute update of the physiological signals of the patients. They also have access to summaries and visualizations highlighting differences between different patient. This information can be used to instantly observe any differences between the hypertensive patients and normotensive control groups (Figures 4.8 and 4.9) .

Figure 4.7: HEAL Dashboard visualizing the physiological signals along with the annotations

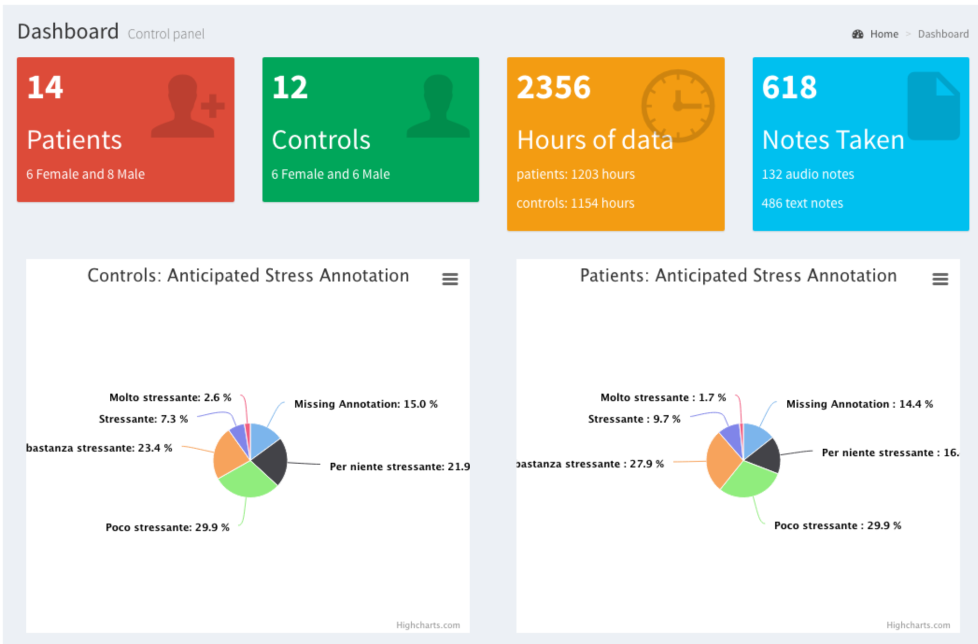


Figure 4.8: HEAL Overview Dashboard for Doctors - the dashboard shows the summary of the hypertensive patients and normotensive controls in the experiment

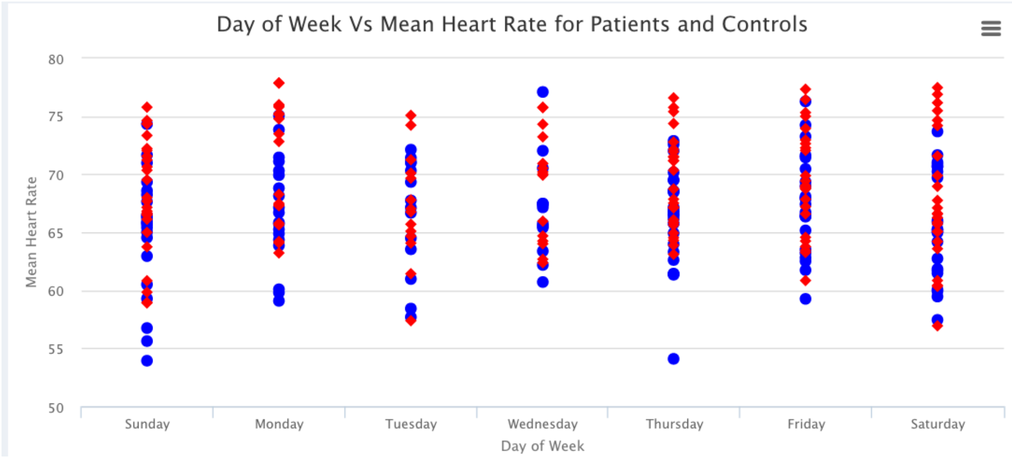


Figure 4.9: HEAL Overview Dashboard showing the mean heart rate distribution of the patient and control groups over days of the week. The RED dots are hypertensive patients and the BLUE dots are normotensive controls

4.6 Conclusion

The Health Analytics (HEAL) platform is a multi-component platform which can help to manage and track various aspects of a chronic disease. In this thesis we apply the HEAL platform for the management of hypertension. In the later chapters we demonstrate how this platform can be used for continuous monitoring of stress in daily life, and can be used also for detecting patients suffering from hypertension.

5

Covert and Overt Signals

In recent years advances in sensor technologies and pattern recognition has made it possible to generate computational models of human behaviour. These computational models have opened up new possibilities of developing advanced commercial, societal, health and educational applications. Building these computational models of behaviour is not an easy task - behaviour is a complex phenomenon which can be affected by both external and internal factors or states of an individual. External factors can be contextual like time of the day, location, environment, company, noise-level, etc. or societal like attitude, perception, culture, and social norms. Internal factors which can affect can affect the behaviour are the psychological or cognitive states of the individual - if the individual is stressed, worried or suffering from some mental condition it can affect the way he or she behaves.

Human behaviour produces both observable and hidden cues. The observable cues of human behaviour generate changes in the produced overt signals - speech, text, gesture, and posture among others. In an interactional scenario these signals are mostly presented with the intention of communication. The hidden cues or the covert signals produce changes to the individual's physiological, psychological and mental state - heart rate, amount of sweating, skin temperature. These hidden or covert signals are indicative of the psychphysiological state or response of a person and are important sources of information for the analysis of behaviour. They signals can be used to determine a person's mental state variables in terms of arousal, valence, or activation, or cognitive load. Identifying these state variables can also be useful for analyzing and explaining the underlying causes of some of the overt responses - such as is the person behaving differently because he is stressed or afraid ?

Both overt and covert signals have been extensively studies in literature for the analysis of human behaviour. Overt signals such as speech and language have been investigated for the analysis of different dimensions of human behaviour. Human speech is an information rich stream with both linguistic and paralinguistic components. While the linguistic part defines the content of the speech, the underlying prosody, speaking style, pitch, accent, stress on certain words can help to identify the emotional and behavioural state of the speaker. Both the linguistic and paralinguistic features of speech have been studied to detect human emotion [157], personality traits[178, 60] and mental state (such as stress level) [161]. Other overt signals such as facial expressions, gaze, posture, and motion patterns have also been well studied for understanding, analyzing and predicting behavioural and mental state. Posture and has been used to gauge socio-emotional states of people such as frustration [153, 78] engagement [226], and attention [164]. Motion patterns such as gross body movements and gesture have also been studied for the detection of frustration [83], and emotions such as fear and anger [76, 56]. Micro changes in facial expression of people observing video streams [185] have been used for detecting emotional responses towards advertisements.

Covert physiological signals have also been used identify an individual's psychological state. The predictive power of physiological signals for mental state has been long exploited in polygraph tests [142] where changes in mental stress due to cheating or lying are reflected through changes in the various physiological signals such as heart rate, electrodermal activity and skin temperature and their combinations. Subsequently in later years, this power of physiological signals to indicate the mental and cognitive state of a person was exploited in different fields of study from healthcare to commerce. Neuroimaging techniques such as EEG, fMRI, and MEG have been used in neuromarketing to detect consumers' brain activity to predict their attitude towards a product [28, 167]. Analysis of electrodermal activity and facial expression has been used to classify response of children suffering from autism spectrum disorder [227]. Behavioural signals such as motion patterns, mobile phone usage, and gesture have been used for detecting conditions such as depression[61], bipolar disorder [33]. Physiological signals such as electrodermal activity (EDA), heart rate variability (HRV), and skin temperature have been used to detect stress [107] and hypertension [109]. Analysis of the EDA of employees has been used to detect stress and performance in call centers [134].

It is difficult to continuously observe and analyze overt signals such as speech, facial expression, and gesture due to limitations of technology as well as concerns of privacy. The recent development in the field of wearable computing on the other hand, has made continuous unobtrusive monitoring of physiological signals possible. Recent large scale adoption of wearable devices has opened up new avenues for research into understanding the mental state of an individual. In this thesis we combine periodic recordings of overt signals (speech/text) with continuous recordings of covert signals (heart rate, electrodermal activity, skin temperature recorded using a wearable wrist-based monitor) to develop algorithsm to identify the mental state of the subjects. In later chapters we use various combinations of these signals to identify stress, workload, and activity of the user - and ultimately we demonstrate how these signals can be used to identify patients suffering from hypertension. In the rest of this chapter we discuss in brief the characteristics of the various covert and overt signals collected in this research.

5.1 Overt Signals

In traditional and controlled research scenarios, multiple overt signals can be recorded and used to observe and identify human behaviour. Signals such as speech, activity, gait, posture, eye-gaze among others have been extensively studied for the analysis of human behaviour in controlled in-lab conditions. In most in-lab experimental scenarios, apart from the technical ease of recording, the privacy issues are also diminished. Since that the experimental subjects are already aware and have agreed to being recorded, it can be argued that within reasonable ethical parameters, the privacy concerns are not high. However, when recording signals in on-the-go realistic scenarios, where the subjects go about in their everyday life, privacy issues can be very high - it is not possible to record any overt signal which might compromise the subject's reasonable expectation of privacy. All recordings under such scenarios should be voluntary in nature, and the subject should be able to review, edit, and delete any such recorded data. Due to these prerequisites of privacy, in this research all overt signals were based on voluntary registration (recording) of the signals by the subjects.

In this work we collect two kinds of overt signals:

1. Structured overt signals: Structured overt signals are responses collected from users through structured questionnaires. For this work, we collect annotations from users based on three different psychological questionnaires.
2. Unstructured overt signals: Unstructured overt signals are richer in terms of content since they allow users to provide more information. In this work we collect user diary annotations as short free-form speech and text annotations from the user.

5.1.1 Structured Overt Signals

Structured overt signals have a predefined standard format. Elicitation of such signals may be through structured interviews, forms or multiple-choice questionnaires. Such signals are extremely important in the field of psychological assessment. Psychological assessment is "the systematic evaluation of a person's behaviour" [128]. It is an important part of many clinical processes and includes several dimensions such as behavioural assessment, personality assessment and social assessment. It can provide underlying information for evaluation of behaviour, analysis of job satisfaction identification of diseases and detection of stress. Questionnaires are a popular method of psychological assessment as they provide a fast and efficient method for collecting large amounts of information from a lot of people. They have been extensively used in psychology for carrying out research for psychological assessment. They are also widely used for research in several domains ranging from marketing to healthcare. In our work we use three types of questionnaires:

Stress Perception Questionnaires

The way a person perceives a stressful event impacts how stress affects the individual's health [166]. Different individuals respond differently to the same stressful event. If one person perceives an event as extremely stressful while another person doesn't, then the effect of the same stress on the latter is much lower than that on the former. Hence the perceived stress scale [69] has become a widely used measure for stress perception and its validity and reliability has been replicated in a large number of studies [26, 70, 71].

In our work we use a stress perception questionnaire which consists of questions about anticipated and perceived stress and workload administered thrice a day.

Emotion Regulation Questionnaire

Emotion regulation refers to the process that individuals use to feel, express, and control the emotions they experience in their daily lives [113]. It is used by individuals to modify their emotional experiences, expressions, and physiology as well as manage the situations eliciting such emotions in order to produce appropriate responses to life events. The emotional reactions to stressful events entail emotion regulation [263].

Two underlying dimensions have been proposed as primary factors of the emotion regulation process - **cognitive reappraisal** and **expressive suppression** [115]. Cognitive reappraisal is an *antecedent-focussed* strategy that acts before the activation of an emotional response, while suppression is a *response-focussed* strategy that occurs when an emotional response has already been deployed. Different individuals use these dimensions differently and this can affect the way they experience and deal with stress in their daily lives. It has been suggested that the suppression strategy may require some effort to manage the emotional response thus reducing the cognitive and affective resources of an individual. It has been shown that use of response-focusses strategies like expressive suppression are correlated with self-reported depression [181].

The emotion regulation questionnaire (ERQ) is a ten item scale [116] designed by Gross and John (2003) to measure how the respondents use cognitive reappraisal and expressive suppression strategies for emotion regulation. Studies using the emotion regulation questionnaire have demonstrated that increased use of expression suppression strategies is linked to mental problems such as anxiety [188], stress[53] and depression[246].

Holme's and Rahe Stress Scale

The social readjustment rating scale [139], more popularly known as the Holme's and Rahe Stress Scale is a list of 43 life-changing events used to generate an overall score for the stress level of a person. It is a widely validated scale and it has been shown that there is a correlation between the score of the stress scale and the occurrence of illness [240, 170].

In this work we use this scale to assess the occurrence of any life-altering stressful events before the onset of the hypertension in the patient group. This scale was also used as one of the metrics to select normotensive subjects - people scoring high on this scale were eliminated from the normotensive group.

5.1.2 Unstructured Overt Signals

Overt signals such as speech and text notes provide information about users which might be otherwise difficult to collect through structured questionnaires. While multiple-choice questionnaires provide a rating, unstructured annotations can provide groundings for those ratings. Written text is more rich in emotional and affective content than structured ratings. They can be analyzed and used as determinants for the communicative, affective, and social behaviour of the author by providing underlying information about his/her mental state. Text messages sent through short messaging services (SMS) or social media status messages have been used to identify personality traits [273, 58] of a person. Written comments have been used to identify opinions and sentiments from customer surveys [250]. Analysis of short unstructured customer product reviews have been shown to be more effective in predicting conveyed sentiment than user-provided ratings [105, 104].

Collection and analysis of user diaries in the form of spontaneous speech and text annotations have been widely used in psychology and organizational research. A fundamental benefit of using such diaries to collect user annotations is that they allow expression of thoughts, feelings, events and experiences in natural and spontaneous manner [217]. Such diaries have been used to study persons' affective states [280], job performance [103], as well as their emotions at work [45].

However, the use of diary studies is not without its difficulties - the significant demands on the participants for regular diary-keeping often leads to a high level of attrition [183]. There is a need for creating a diary recording process which is easier and more straightforward for the subjects, while at the same time increases the richness and quality of the collected content. One way of achieving this is using audio or speech based diaries.

Audio diaries involve the audio recording of participants' responses, notes and reflections which serve as a verbal monologue [51]. With the recent development of smartphones which can capture audio data easily without the need of any additional recording device, audio diaries have become easy to use and have gained a wider acceptance and popularity [160]. The speech recorded using these diaries can be easily transcribed using speech to text services for further analysis of the content. The features of the speech signals themselves can be indicative of the emotional and mental state of the user.

In our research we collect spontaneous speech and text diaries to help us to understand and ground the other covert signals collected.

5.2 Covert Signals

In this work the covert signals analysed were either physiological - electrodermal activity (EDA), heart rate variability (HRV), and skin temperature (ST), or corresponded to the motion profile (from an accelerometer and a gyroscope) of the user. These signals were collected using the sensors on a wrist based wearable devices and a user's smartphone. While physiological signals help to detect the stress level of the user, the accelerometer and gyroscope signals are used to identify the activity profile of the user.

5.2.1 Covert Physiological Signals

Research in psychophysiology and affective computing have demonstrated how affective and cognitive states manifest themselves through changes in the human physiology [54, 203]. Studying physiological signals can help in creating computational models of the human mind. Emotion [72, 211, 86], stress [30, 130], and workload [132] are intrinsically tied to the activity of the autonomic nervous system (ANS). Empirical evidence has shown that sympathetic activation of the ANS which occurs during stress and anxiety and in some diseases (eg. cardiovascular disease) is manifested through changes in the human physiology [43, 159, 168]. These changes can be detected by observing changes in physiological signals like electrodermal activity (EDA), heart rate variability (HRV) and skin temperature (ST).

Electrodermal Activity

Electrodermal Activity (EDA) refers to the change in the electrical property of the human skin. The electrical property of the skin was observed for the first time in 1849 by DuBois-Reymond in Germany. In 1878 , Hermann and Luchsinger of Switzerland demonstrated that this property was linked to the human sweat glands. In the same year a French electrotherapist Romain Vigouroux discovered the relationship between psychological factors and the electrodermal activity of the skin. In 1888, the French neurologist Féré demonstrated that emotional stimulation produced changes in the skin resistance activity. Since then it has been widely used in psychological research.

Historically electrodermal activity has been referred to by various names such as galvanic skin response (GSR), electrodermal response (EDR), and psychogalvanic reflex (PGR). In 1966 Johnson and Lubin [147] introduced electrodermal activity (EDA) as a common term for all the electrical properties of the skin.

Electrodermal activity (EDA), or the changes in the skin's electrical property in caused due to the activation of the sweat glands in the skin. This activity is a normal part of the process of homeostatic thermal regulation by the human autonomic nervous system. The sweat glands are also activated under various emotional or psychophysiological changes in the body, particularly due to increase in stress or arousal. Measurement of electrodermal activity for identifying emotional arousal has been used in research for the detection of affective scenes in movies [244], for the identification of user response to listening to music [225], and detection

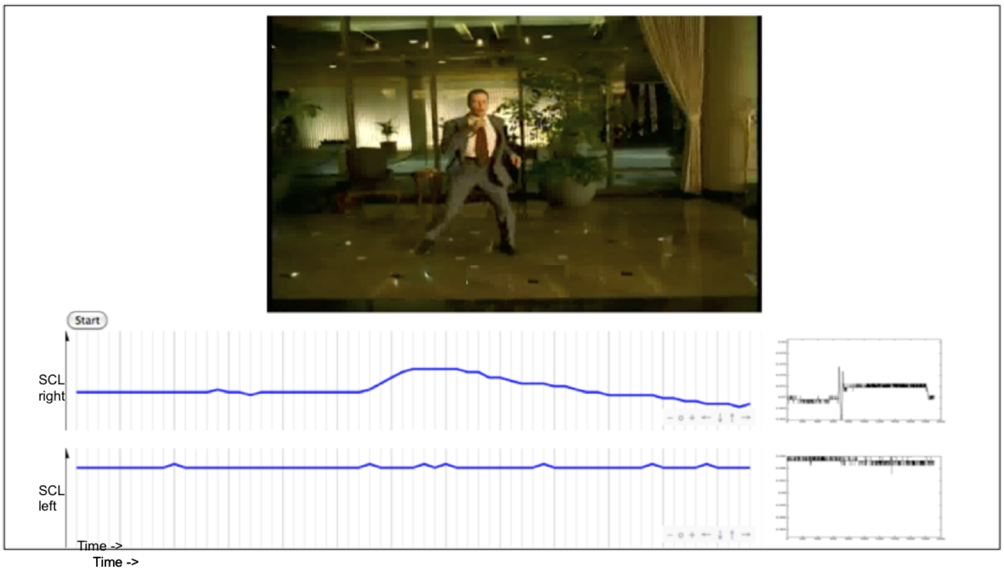


Figure 5.1: Changes in skin conductance level for affect detection in movie scenes

of driver fatigue[52]. Figure 5.1 shows an example of changes in the skin conductance levels on the forearm during movie scene viewing.

There are two main components of EDA, both of which have been shown to provide high discriminatory power for different levels of arousal, stress and workload. The *tonic EDA* or the skin conductance level (SCL) is the baseline level of EDA in the absence of any external stimuli. Every person has a distinct tonic EDA which ranges typically between $10-50\mu Seimeins$. *Phasic EDA* or the skin conductance response (SCR) is the rapid change in skin conductance due to sympathetic neuronal activity. This change could be due to external physical changes (shock, heat, cold, fall) or due to emotional or cognitive changes (surprise, fear, anxiety etc). SCRs usually are short-term and last between 10 and 20 seconds followed by a return to the tonic or baseline level of skin conductance (SCL) (See Fig.5.2).

Both distress (negative stress) and eustress (positive stress) which cause changes in the autonomic measures of the nervous system, are manifested through changes in the electrodermal activity. For long, EDA has been used for studying mental stress and is one of the main physiological signals used in a polygraph [123]. Due to the ease of acquiring EDA, it has also been applied for stress recognition in real-life scenarios ranging from

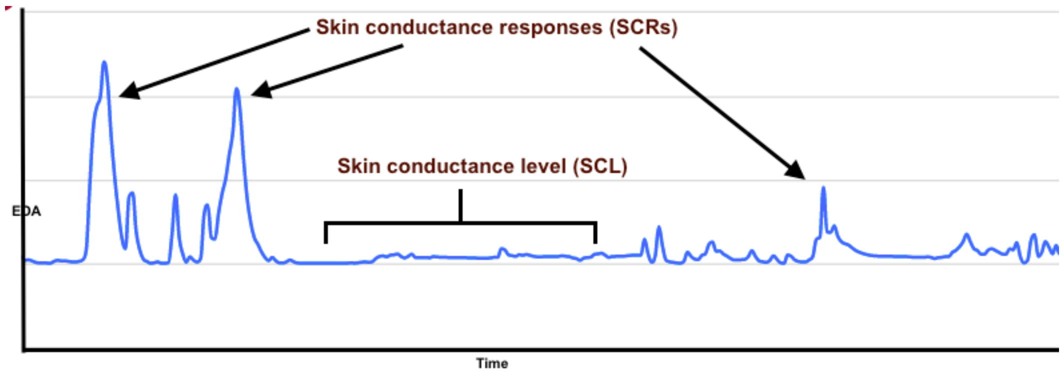


Figure 5.2: Skin conductance level (SCL) and skin conductance responses (SCR) in a longitudinal Electrodermal Activity recording

driving [130] to job related stress recognition [30]. Electrodermal activity has been shown to be sensitive to cognitive load in real-life conditions [132]. Rutenfranz and Wenzel [47] showed that increase in either physical or mental workload led to changes in the electrodermal activity. Engstrom et al. [89] showed that mean skin conductance significantly varied with increase in cognitive load during driving scenarios. EDA has also been used for emotion detection [198]. A detailed discussion of the literature of electrodermal activity and techniques for its measurement is provided in [47].

In this work we find that Electrodermal Activity is an important indicator for stress. Combined with other physiological signals we use it for the identification of hypertensive patients.

Heart Rate Variability

Heart Rate Variability (HRV) is the measure of the variations of the time-interval between heart beats. These variations are produced by the change in the modulation of the sympathetic control of the heart and can be used as a non-invasive technique to examine autonomic nervous function [23].

These variations can be evaluated by using time-domain or frequency domain measures. The simplest measure, the detection of the instantaneous heart rate is one of the most common methods used in clinical and everyday practice for understanding the state of a patient. Using an electro-cardiogram (ECG) or photoplethysmograph (PPG), it is possible to analyze longer segments of heart rate variability features. The recommendation for clinical analysis of HRV is to use data from a 24-hour ECG or holter based recording. However, short-term HRV features of as low as 10 minutes have been shown to be highly predictive of hypertension [196]. Short term HRV analysis is a major indicator of the risk of sudden cardiac death in chronic heart failure patients [162]. HRV features can be extracted from a recording of blood volume pulse (BVP) from a pulse oxymeter, or the recording of an ECG signal.

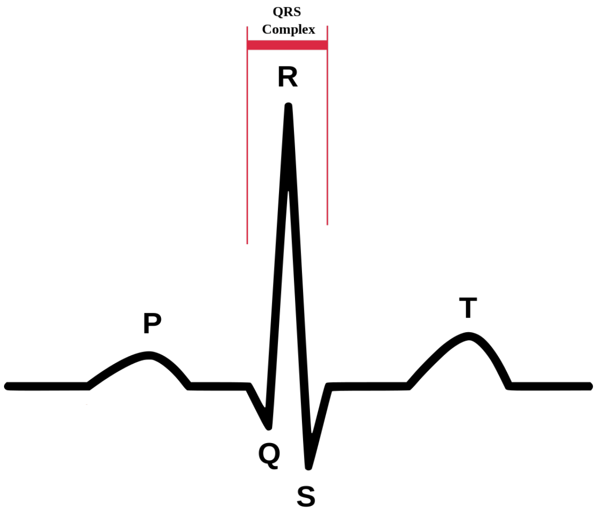


Figure 5.3: Detection of QRS complex

For the analysis of the HRV, the first step is the identification of the N-N interval from which other features are extracted. From an ECG, or BVP signal, first the QRS complex is detected 5.3, and then the distance between two consecutive QRS complex is determined 5.4. This distance or interval between two consecutive QRS complex is called the N-N interval (or R-R interval).

Next features are extracted from the sequence of N-N interval

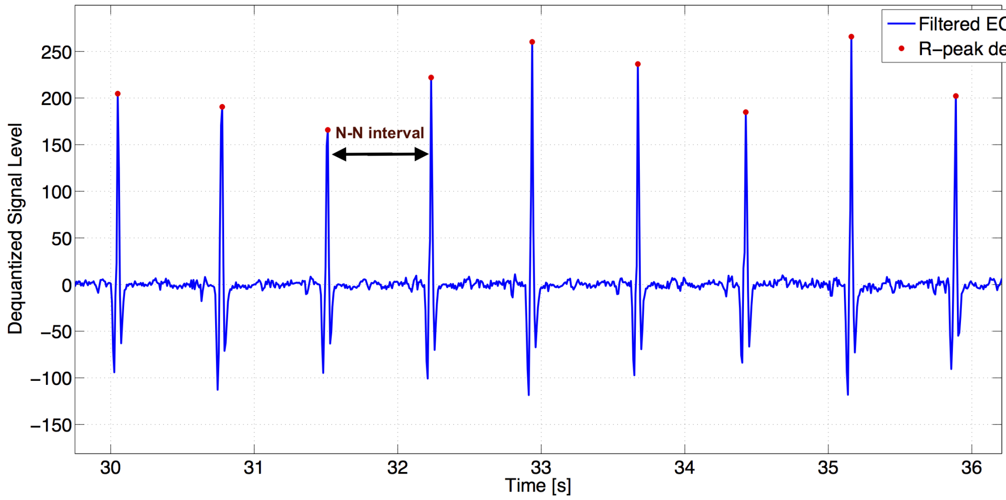


Figure 5.4: Identification of N-N Intervals from ECG signal

datapoints. Popular time-domain measures of the heart rate variability are mean heart rate, mean N-N interval and the standard deviation of the NN interval (SDNN). Differences between N-N interval yield measures such as root mean square of standard deviation (RMSSD), which is the square root of the mean squared differences of successive N-N intervals. Other statistical features such as pNN30 and pNN50 which represent the percentage of N-N intervals greater than 30 or 50 ms respectively are also calculated.

HRV is indicative of the heart's ability to adapt to the autonomic neural regulation. Events and conditions such as exercise, stress, workload, anxiety and cardiovascular diseases which lead to sympathetic stimulation has been shown to increase the heart rate while decreasing it variability. A reduction of heart rate variability has been linked to a poor prognosis of several clinical conditions. In 1965 Hon and Lee [141] observed a decrease in the inter-beat interval value of HRV as a signal of fetal stress. A reduction of HRV has been accepted as a correlate for stress among individuals [37], and in several cases is associated with increased mortality and morbidity. Reduced HRV has been shown to be correlated with an increase in risk in cardiovascular mortality [259, 201].

In this thesis we analyze the heart rate variability features and discover that simple time-domain features such as average heart rate, and mean N-N interval differ between hypertensive and normotensive subjects.

Skin Temperature

The normal temperature of the human body is 98.6 degrees fahrenheit (37 degrees celsius). However, it is not uniform throughout the body and shows a standard variation of 2 to 4 degrees at different surfaces. Variations in the skin temperature is a part of the body's normal thermo-regulation process and occur due to a combination of perspiration and changes in the vascular resistance or arterial blood pressure.

The core body temperature can be recorded from the oesophagus, pulmonary artery or urinary bladder [236]. However, the methods required for measuring temperature from these sites are quite invasive and hence difficult to implement. For everyday monitoring, the peripheral temperature is recorded from the surface the skin. While the core-body temperature is tightly regulated, peripheral temperature varies due to changes in environmental as well as health factors. Monitoring and control of peripheral body temperature has been used to prevent hyperthermia (overheating during hot temperatures, and extreme physical activity) or hypothermia (overcooling due to exposure to cold temperatures).

In our work skin temperature when combined with other physiological signals demonstrates improved predictive power for classifying between low and high stress.

5.2.2 Motion Profile

Most modern smartphones come equipped with accelerometer and gyroscope motion sensors. The accelerometer sensor detects the motion - it measures the linear acceleration of movement. The gyroscope sensor detects the angular motion. Most accelerometer and gyroscope sensors measure these values (acceleration and rotation) along the three axes and hence are called tri-axial accelerometer or gyroscopes. The accelerometer sensor is normally used to detect the orientation of the phone, or shake to undo, etc. The gyroscope sensor works with the accelerometer to detect rotation or twist. These sensors can be used to detect when a phone is falling, or whether the user is interacting with the phone. We show that these signals can be used to identify the user's motion activity (such as walking, running, cycling, etc). We use a combination of features extracted from the accelerometer and gyroscope to train advanced machine learning models to accurately estimate a user's motion activity. We show that adding the audio sensor makes it possible to identify and distinguish between complex and similar activities.

In our work we use combinations of the above physiological signals and motion sensors to build intelligent algorithms for assisting a mobile personal agent in learning about the physical and mental state of the user.

5.3 Conclusion

In this chapter we discussed the various covert and overt signals which are indicative of human behaviour. We provided a brief introduction to and the history of the use of each type of signal we shall use in our research. We discussed that these signals have been used separately and in-combination to detect and analyze complex human behavioural and mental states. In later chapters we shall demonstrate how these covert and overt signals can help to identify activity and stress levels. We also demonstrate that combination of the various covert signals can accurately identify hypertensive patients.

6

Recognizing Human Activities

6.1 Introduction

Our daily activity patterns highly affect our health and well being. It is well known that lack of adequate physical activity can lead to obesity, and increases the risk of various diseases including hypertension, cardiovascular diseases among men [264] and coronary artery disease among women [84]. Research has demonstrated far reaching effect of physical activity which affects our entire body system. Regular physical activity in the form of exercise is known to reduce resting blood pressure [216] and increase the capacity of coronary arteries to carry blood [256]. Physical exercise has often been prescribed for prevention and reduction of the risk of cardiovascular diseases, type 2 diabetes, depression, hypertension and obesity [35, 49].

While physical activity in terms of exercise is beneficial to our health, certain activities such as our daily commute can have the exact opposite effect on our health. How and when we travel can affect our overall mental an physical well-being. Travelling to work by a crowded bus, or biking in heavy traffic may have negative effects on the mental health and decrease well-being. Traffic congestions which can increase the length of the commute have been shown to elevate psychophysiological stress [228].

Among automobile commuters this effect has been shown to extend beyond the period of commute - it has been shown to decrease affective well-being even after the commute [202]. Commuter stress has been highly linked to workplace aggression [133]. The modality of transport also affects the stress of commute. Both driving a car [117] or taking a train [239] to work has been shown to increase the stress response of an individual. Travelling by bus is less stressful than either driving or taking the train, but longer commuting time can increase the exposure to environmental pollutants thus in turn increasing the chances of respiratory diseases. Longer commuting time, whether it is by bus or train also decreases the tolerance for frustration [269]. It has also been shown to raise daytime cardiac autonomic activity and short-term heart rate variability [149]. The recognition of daily user activities is therefore an important task for tracking and managing stress and overall well-being of a user.

6.2 Activity Recognition Techniques

In recent years, the development and proliferation of various sensor platforms has given rise to the field of automatic activity recognition. Automatic activity recognition aims to identify the current activity of a user through the use of various sensors and algorithms. Activity recognition systems may be vision based, sensor based or hybrid (combination of the two). Vision based systems use external cameras [267] to monitor the users. This can often limit their usage scenario to cases where the user can be observed - such as indoor or controlled environment. This also raises the question of user's privacy - users may not be comfortable being recorded.

Sensor based activity recognition systems, use various sensors (external and wearable) to recognize human activities. They are less privacy intrusive than vision based activity recognition systems. External sensors may be based on infra-red sensors which use heat signatures for activity recognition[122] or be based on doppler-effect using a doppler radar to detect activities [155]. However, like vision based systems, they are effective in specific scenarios (where the system is aware of the user's position - hence mostly in indoor or controlled outdoor environments) and can have limited usability in on-the-go scenarios where the user is free to go anywhere.

To tackle these mobility challenges of external sensor based activity recognition systems,there has been a recent rise in the use and adoption of wearable sensor based systems. These wearable sensor based systems are on the body of the user, and hence can monitor users in unconstrained environments. Till recent years in most wearable sensor-based approaches, users had to attach multiple dedicated motion sensors [182] to various parts of the body such as legs, arms, and waist. While such systems have been able to achieve high recognition performances, they require elaborate set up and can be uncomfortable to wear and hence are not very suitable for long-term monitoring. These systems also have other drawbacks.

Due to the traditional method of in-lab evaluation of activity recognition systems, most of them suffer from the drawback of failing in real-life scenarios. While in controlled experimental scenarios, most activity recognition algorithms perform quite well, in naturalistic settings the performance drop drastically. Foerster et al. in [97] achieved a 95.6% accuracy for in-lab detection of nine different activities (3 different modalities of sitting, standing and lying, walking, climbing stairs and cycling) using four sensors attached to different parts of the body. However, when the same setting was used in the wild, this accuracy fell down to 66%.

6.2.1 Smartphones for Activity Recognition

The recent proliferation of smartphones with their plethora of sensors have opened up a new frontier in context aware human computer interaction. Most modern smartphones have embedded sensors such as microphone, camera, accelerometer and gyroscope. Accelerometer and gyroscope sensors have been successfully used to detect human activity [27], understand human mobility patterns [64], and monitor Activities of Daily Living [279]. Scientists have also exploited the microphone on smartphones for daily activity recognition. The SoundSense [173] project used the microphone on a smartphone for detecting and modeling sound events in everyday life. Bieber et al [40] combined the accelerometer and microphone sensors for detecting everyday activities. Schuller et al in [232] used the microphone of a smartphone for acoustic geo-sensing to automatically determine a cyclists route.

However, smartphone sensors are not robust, and performance of a single-sensor based classification systems leads to sub-optimal and non-robust performances. The quality and response of on-board accelerometer and gyroscope sensors vary across manufacturers and devices. Certain smartphones do not have dedicated gyroscope hardware, and implement it in software propagating errors from accelerometer into gyroscope readings. The accelerometer performance for activity recognition task degrades rapidly when the user is playing a game on the smartphone or using an application. Similarly, as reported in [173] audio data cannot be the sole source of information when the phone is in a backpack or the user is on a call. The solution is to use multiple weak signals and combine them to improve the recognition of a user's activity state. Combining multiple sensors can also lead to opportunistic sensing, thus improving the energy consumption of the phone by smart decisions on turning on/off sensors at appropriate times.

Proper evaluation of an activity recognition system is another challenge. Although activity recognition using smartphone data is a popular research field, very few publicly available corpora have raw data available. Among those available, most of the corpora were created under controlled environments with static phone placements, or scripted activities where the user does not otherwise use the smartphone during the data collection. Therefore in this work we carried out our own data collection on the Android and iOS platforms in a naturalistic settings. We also collected a smaller "stress-test" corpus where the data was collected while the participants were actively using the phone. We develop an activity recognition algorithm for detection of the modality of commute and whether the user is sedentary. We use these two factors in Chapter 7 for the recognition of the stress level of an individual.

6.3 HEAL Activity Recognition Experiments

The HEAL platform collects and analyzes data from a variety of sensors. Among these, the data from the accelerometer and gyroscope sensors of the iPhone are also recorded. In this chapter we describe the use of these signals for developing advanced activity recognition algorithms for the continuous monitoring of users/patients.

To develop the activity recognition algorithm for recognition of human activity in the wild, we performed a set of targeted data collection and analysis. The data from the various sensors were combined to come up with an effective algorithm that is accurate as well as efficient. In the following sections we discuss the data collection, experiments, and analysis.

6.3.1 Data Collection

The goal was to develop an activity recognition algorithm which can be used in the wild. We performed two different sets of data collection experiments for our system. Each experiment involved 15 (9 male and 6 female) participants. Participants varied in age between 25 and 40. The devices used were smartphones running android [1] (10 participants) and iOS[2] (5 participants) operating systems. Participants were located in various cities in Italy, Spain, and India, thus providing our data a wide geographic variability. The participants were provided with a mobile application 6.1 which they installed on their phones. While a separate application was developed for each platform, both applications had the same functionality and recorded data from the same set of sensors. The applications sampled the tri-axial accelerometer sensor, gyroscope sensor,

[1] version 4.0 and higher
[2] iOS 6 and higher

location sensor, and microphone during the data collection phase.

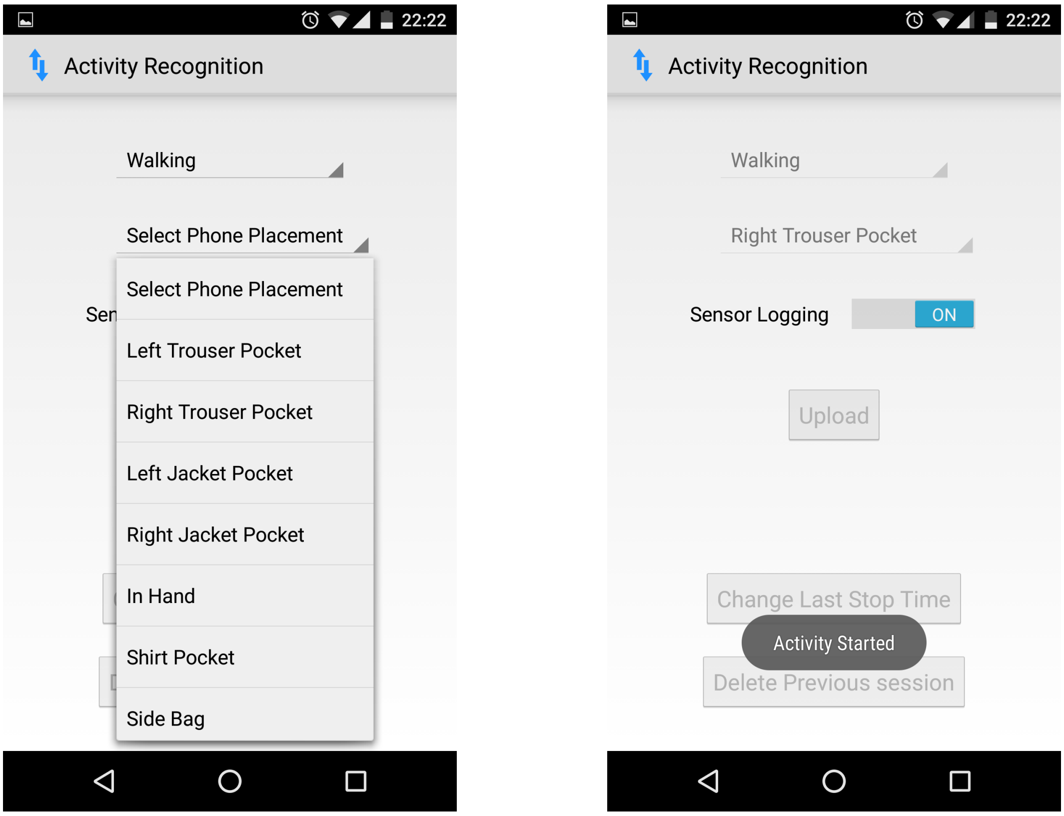


Figure 6.1: The Activity Annotaion Application - This application was used for the collection of in-the-wild activity annotations from users.

The data from the following sets of sensors were collected:

1. accelerometer at 40 Hz
2. gyroscope at 40 Hz
3. audio was recorded with a 8 KHz sampling rate
4. Location data was collected at the rate of 1 sample per 5 minutes

The location data was used only for validation and was not a part of the activity recognition process. Also, the participants often turned off location service on their phone to decrease power consumption.

Semi-controlled data collection

The first data collection experiment was a controlled scenario where the participant did not interact with the phone during the duration of the experiment. Data was collected for six activities. The activities are *Walking, Standing, Sitting, Driving, Travelling by bus, and Travelling by train.*

The data collection protocol involved the following steps:

1. The participants launched the application before the start of the activity.
2. The participants marked the activity start point on the application.
3. The participants annotated where the phone was carried.
4. The participants marked the end point once the activity was over.

Participants were free to carry the phone as they wanted, but had to annotate the phone placement (pocket, purse, in hand, etc) at the start of the activity using a multiple choice drop-down in the application 6.1. The participants were asked to upload the data to the HEAL servers at the end of the day.

From the collected data we observe that in the majority of cases, the phone was carried on the body (front or back trouser/jacket pocket), with three instances of the phone being placed in the purse. We ignored two instances where the participant was sitting and the phone was kept on the table.

Since we collected the audio data during the process, in order to respect the privacy of the participants, they were provided with the option to delete the recorded session. The participants were free to delete sessions in case there was any undesired characteristic to the data. This could include personal data (audio, location) which the participants did not wish to share.

We collected approximately 31 hours 35 minutes of data (See Table 6.1), with each individual activity session ranging from five minutes (mostly walking) to one hour (commuting). Examples of collected data can be seen in Figures 6.2, 6.3 and 6.4. While the difference between walking and the other two activities is quite clear from only the accelerometer signal, the gyroscope data helps to distinguish (even visually) between driving 6.3 and travelling by bus 6.4.

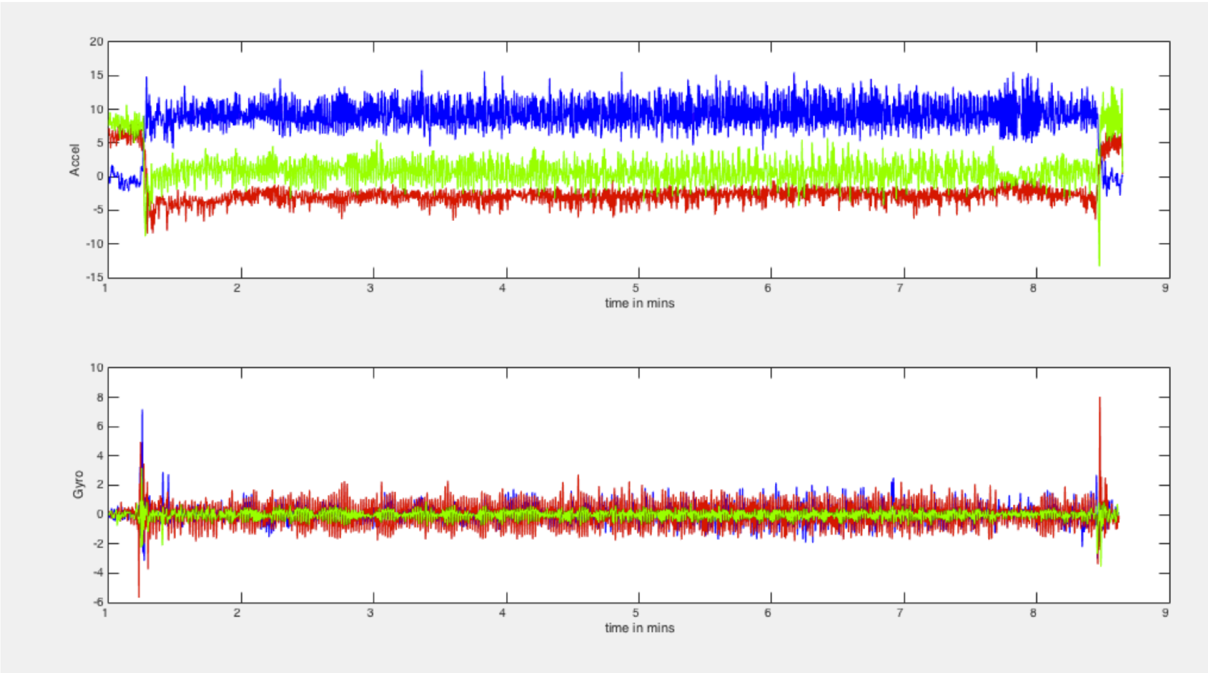


Figure 6.2: The accelerometer and gyroscope signals from an example session while walking

Walking	Standing	Sitting	Driving	By Bus	Train
4.12	8.31	8.23	3.13	2.19	5.12

Table 6.1: Activity Distribution in hours for **normal activities**. The participants placed the phones in pre-defined positions and did not interact with the phone during the experiment. Reported numbers are in hours.

In-the-wild data collection

For the second data collection, our goal was to collect data while the participants were actively using the phone. Most activity recognition

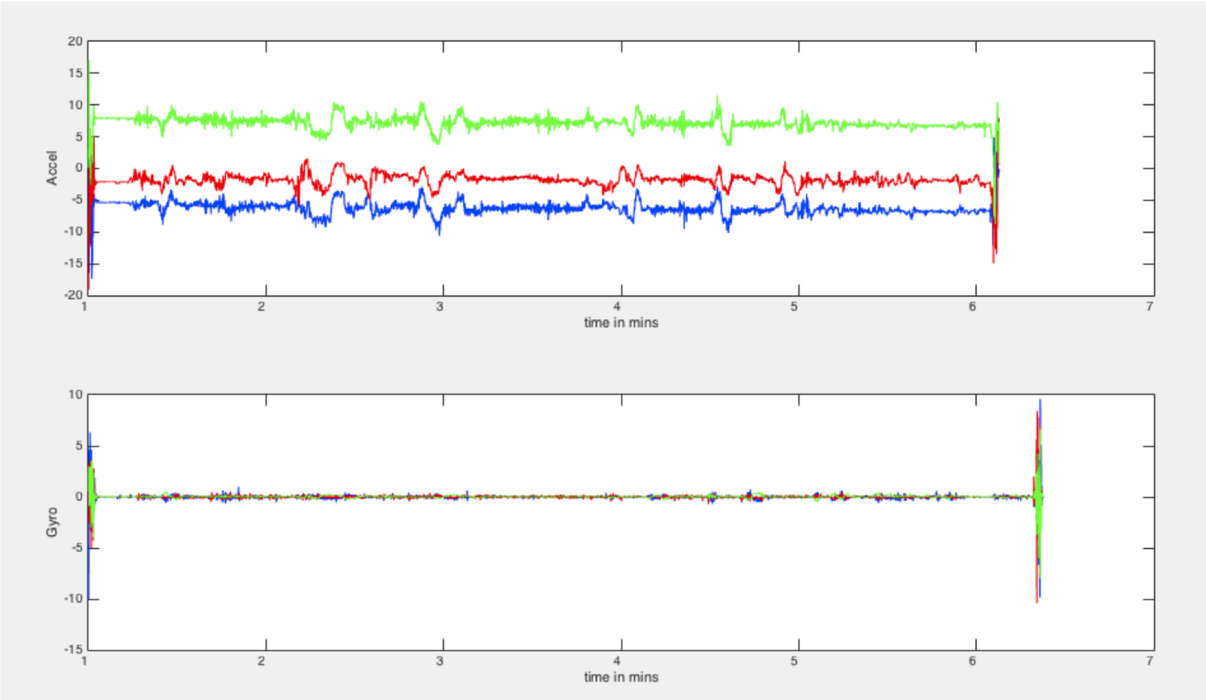


Figure 6.3: The accelerometer and gyroscope signals from an example session while driving

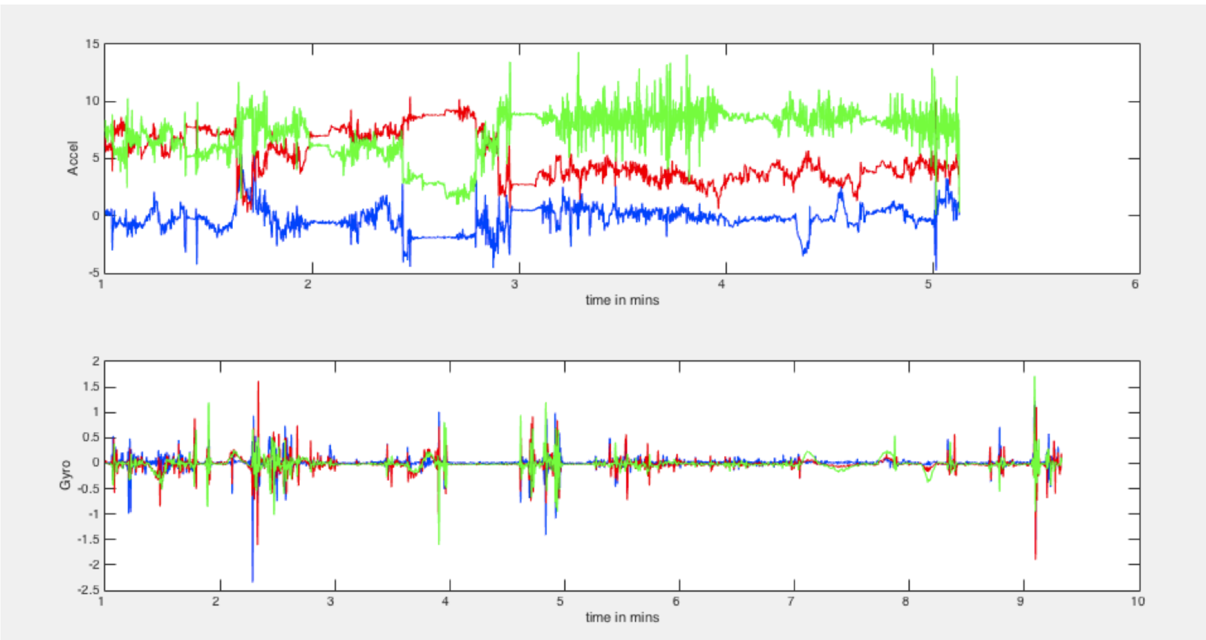


Figure 6.4: The accelerometer and gyroscope signals from an example session while travelling by bus

Walking	Standing	Sitting	By car	By Bus	By Train
0.32	1.21	3.23	2.19	2.47	1.3

Table 6.2: Activity Distribution for **noisy activities**. The participants were actively using their phones(playing games,texting or typing emails) during this experiment.Reported numbers are in hours.

experiments using smarphones have low performance in real life scenarios because they ignore the fact that people interact with their smartphones. During this data collection, the participants were asked to play games or type email or use text messaging services for the duration of the data collection. We replaced the driving scenario with *Travelling by car* during this experiment to ensure the safety of the participant. Approximately 10 hours of data (See Table 6.2) was collected for this scenario.

6.4 Experiments and Results

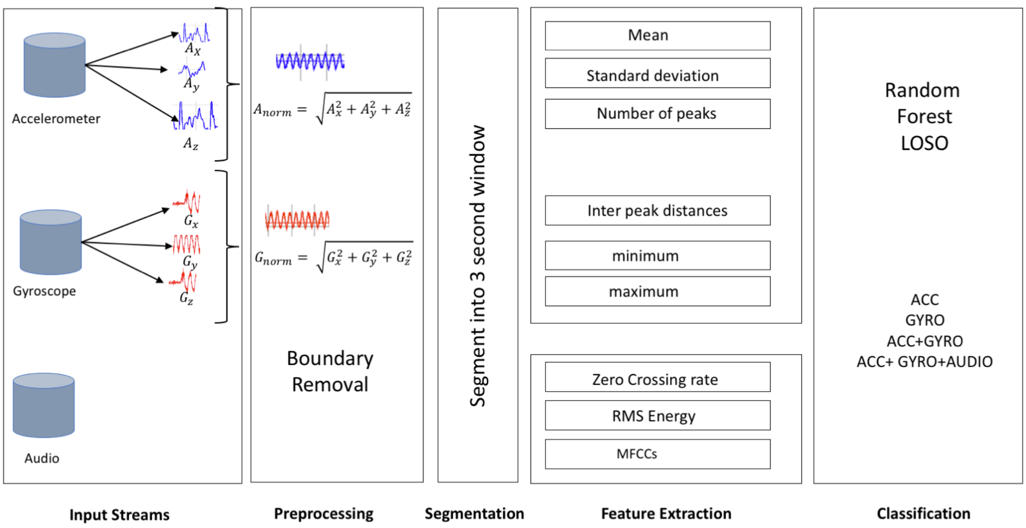


Figure 6.5: The process diagram. The embedded smartphone sensors record data and stream them to the server where pre-processing, segmentation, feature-extraction, and classification steps are performed.

The Figure 6.5 displays the entire process diagram of the HEAL Activity recognition system. Once the initial signal streams are acquired they go through four stages a) preprocessing b) segmentation c) feature-extraction and d) classification for the recognition of the activities. The steps are explained in detailed as follows:

6.4.1 Preprocessing

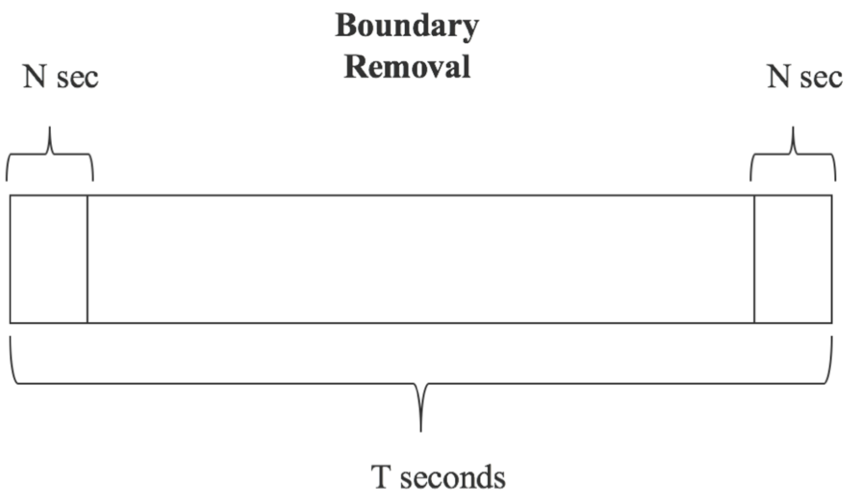


Figure 6.6: Boundary Removal - remove the first and last N seconds where N depends on the total length T (as given by equation 6.1)

The first step in the algorithm was the preprocessing of the data to remove unwanted noise from the beginning and end of each activity session. Since in most cases, there is a lag between the time the user annotated the start of the activity and when the activity actually started, we remove the first and last few seconds of the data. This boundary removal 6.6 involved the removal of the first and last N seconds of the data. N was taken at T/10 seconds with a max value of N=30 seconds where T was the duration of the activity session (see equation 6.1). We only consider sessions which lasted at least 5 minutes for our experiments.

$$N = \begin{cases} T/10, & \text{if } N < 300 \\ 30, & \text{otherwise} \end{cases} \tag{6.1}$$

6.4.2 Segmentation

A big challenge for activity recognition algorithms is effective segmentation of sessions. While longer sessions lead to very good activity recognition performances, uses them means that there will be a delay in the activity and it its actual recognition. This delay will add on top of the usual network, and algorithm processing delays. Due to this an effective window needs to be identified. We experimented with different window sizes and selected a three second sliding window with 50% overlap. This window size has also been established in literature [27, 218] to achieve superior performances for the activity recognition task using smartphones.

6.4.3 Feature Extraction

Next we extract features from each of the three collected signal streams a) Accelerometer b) Gyroscope c) Audio sensors.

Accelerometer and Gyroscope

Accelerometer and Gyroscope sensors each have 3 axes *x,y,z*. The sensor data records the signal streams of these three axes. We first compute the acceleration magnitude, given by:

$$A_{norm} = \sqrt{{A_x}^2 + {A_y}^2 + {A_z}^2}$$

Now for each of the x, y, z, axes and norm of the accelerometer and gyroscope data we extract standard features for each 3-second window. We calculate the mean, standard deviation, min, max, number of peaks, number of zero crossings, inter-peak distances, etc for each of the accelerometer and gyroscope axes.

Audio

We use the same window size for processing and extracting features from the audio signal. While extracting features, we segment the audio stream into small uniform frames. Standard frame-sizes for audio processing lie between 25-46 milliseconds. In our case we use a 23 milliseconds half-overlapping subframes of audio as used by McKinney et al [187].

For the audio signal, we use Opensmile [91] to extract features. The following are the main features for each window:

1. Zero crossing rate - ZCR is defined as the number of time-domain zero-crossings within a frame.
2. RMS Energy - We use the Simple Moving Average of the mean, standard deviation, skewness, max, min, and range of the RMS energy of each window.
3. MFCCs which are very commonly used in Speech and Speaker recognition, have been recently used for recognition of environmental Sound [66]. We use the Simple Moving Average of the mean, standard deviation, skewness, max, min and range of 12 MFCCs for each window.

Durrent et al. [82] defines sensor fusion configuration as complementary if the sensors do not directly depend on each other. While older smartphones use a software gyroscope, modern smartphones (which were used for our experiments) have a dedicated gyroscope chip. So in our experiment we treat the sensor channels as complimentary and use the absolute time for each sensor event (recorded during our data collection) to align the data. We perform a feature-level fusion (early fusion) of the different streams by concatenating the time-aligned feature sets before the learning stage. For each classification experiment we perform feature-vector normalization before training. For each window, all feature-vectors form a $m \times n$ matrix where m is the *window size* $\times$ *sampling rate* for that window and n is the *length of each feature vector*.

Signal	Acc	Gyro	Audio	Acc & Gyro	Acc Gyro & Audio
SVM	0.85	0.79	0.79	0.87	0.91
Decision Trees	0.85	0.82	0.83	0.85	0.90
Random Forest	**0.91**	**0.84**	**0.85**	**0.93**	**0.98**

Table 6.3: Average F-measure of 15-fold (one-fold-per-user) cross validation for the classification algorithms tested with the full feature set with data sampled at 40 samples/second and a 3-second sliding window

For each feature f_{ij} in the feature vector where i=1 ... n is the number of the feature ,and j is the jth row we normalize the feature using:

$$f_{ij} = \frac{f_{ij} - Min(f_{ij})}{Max(f_{ij}) - Min(f_{ij})}, i = 1 \dots n; j = 1 \dots m$$

6.4.4 Classification and Results

For the recognition of the activities, we perform a classification task using the above defined features. We tested three different classifiers : Support Vector Machines, J48 decision trees, and random forests. Random forests provided us with the best F-measures (see Table 6.3), hence further classification was done with random forest for the different sets of experiments. For all classification experiments results were obtained by 15-fold (leave-one-subject-out) cross validation where each fold corresponds to the data for one subject. We used the full feature set with data sampled at 40 samples/second.

A major problem with using sensors on smartphones is that polling them continuously can lead to power drain. Krause et. al in [158] had shown that sampling rate of sensors has a direct effect on the battery life of a wearable device and decreasing sampling rate lowers power consumption. One of the goals of our experiment was to determine how gracefully the recognition quality decreases when the sampling rate is decreased. Since Random Forest was found to provide the highest recognition results for the full samples, further experiments were done using this algorithm.

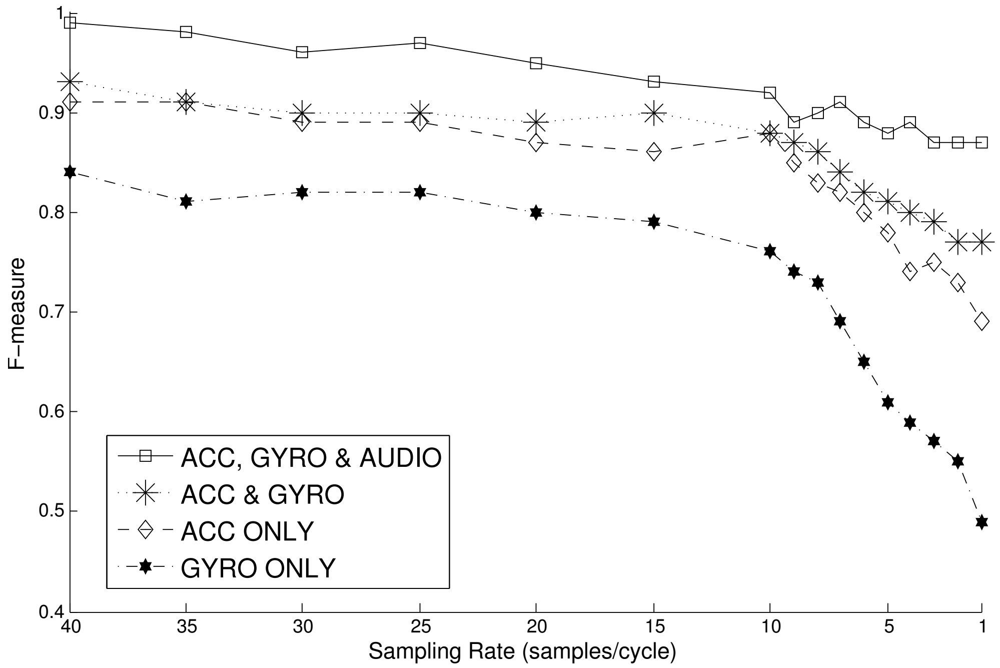


Figure 6.7: Effect of stepwise decrease of sampling rate (from 40 to 1 samples/sec) on F-measure. We see that adding audio leads to better accuracy at lower sampling of acc and gyro sensors.

We performed stepwise downsampling of the accelerometer and gyroscope signals from 40 sample/sec to 1 sample/sec. From Figure 6.7 we see that accelerometer performance(F-measure) drops from 0.91 to 0.69 when the sampling rate is decreased from 40 to 1 sample/sec. Gyroscope performance (F-measure) drops more steeply from 0.84 to 0.49 in this range. A combination of Accelerometer and Gyroscope fairs comparatively better, degrading from 0.93 to 0.77. Adding audio signals from the microphone not only helps to provide better results at higher sampling rate (0.98 at 40 samples/sec), but also helps to balance the drop to only 0.89 at the lower end. However, we did not experiment with different sampling rates of the audio because of the limitation of the audio format for recording. AAC audio coding, which is the standard audio codec on both iOS and android does not support compression below 8 kHz. So all experiments with audio were carried out at this sampling rate.

From Table 6.4 we see that under controlled experimental conditions, accelerometer performance can be a good measure for understanding a

Signal	Average precision	Average Recall	Average F-measure
Acc	0.90±0.02	0.91±0.03	0.91±0.03
Gyro	0.83±0.08	0.84±0.07	0.84±0.08
Audio	0.85±0.06	0.86±0.07	0.85±0.07
Acc Gyro	0.93±0.06	0.92±0.06	0.93±0.06
Acc Gyro Audio	**0.98**±0.05	**0.97**±0.05	**0.98±0.05**

Table 6.4: Average Precision, Recall and F-measure using random forests. For this experiment the participants were requested to place the phones at pre-defined location and not use it during the experiment

participant's current motion profile. In this experiment the participants were expected not to interact with the phone for the duration of the experiment. While post-processing we ensured that we removed all instances where the screen of the phone was unlocked for durations longer than 10 seconds during a data collection session since it indicated that the participant was using the phone. However, since the participants were free to carry the phones as they wanted, this data collection is less controlled than other controlled data collection [27, 64] for activity recognition.

Table 6.5 shows the recognition results when the participants were actively using the device phone while performing an activity. Average precision for single sensor channels is lower than in the controlled experiments reported in Table 6.4 . The accelerometer and gyroscope individually perform lower (F-measures 0.76 and 0.72 respectively) than in the controlled scenario (F-measures 0.91 and 0.84 respectively). While combining the two sensor streams improves the recognition rates (F-mseasure 0.80), combining the motion sensor channels with audio achieves the best results (F-measure 0.87) under this scenario.

6.5 Conclusions

In this chapter we have explored the use and combination of multiple weak smartphone sensors. We show that while activity recognition performance using smartphone sensors drop heavily during real-world usage, combining

Signal	Average precision	Average Recall	Average F-measure
Acc	0.75±0.13	0.77±0.10	0.76±0.11
Gyro	0.70±0.17	0.74±0.16	0.72±0.16
Audio	0.85±0.08	0.85±0.09	0.85±0.08
Acc Gyro	0.79±0.13	0.80±0.12	0.80±0.13
Acc Gyro Audio	**0.86±0.11**	**0.88±0.11**	**0.87±0.12**

Table 6.5: Average Precision, Recall and F-measure of sensor channels using random forests. For this experiment the participants were actively using the phone during data collection

multiple signal streams can lead to better recognition results. We show that by using a combination of features from accelerometer and gyroscope signals we can achieve a high recognition rate in real world scenarios. If we also exploit the less-used microphone sensor on a smartphone we can achieve an even higher recognition accuracy. By combining audio features with other weak sensor features we can come up with a robust activity recognition scheme. We use the activity recognition algorithm in the next chapter for classifying the activity level as a step towards stress recognition.

7

Identifying and Tracking Stress and Workload

Stress is a complex phenomenon which plays an important role in our daily lives. It has become a common explanation for disturbed human behaviour, failure and psychological breakdown among people. Stress plays a very important role in the management of hypertension. According to a recent report by the European Agency for Safety and Health at Work (EU-OSHA) [127], stress is the second most frequent problem among European workers after musculoskeletal disorders. Stress affects one in five of the working population irrespective of their job roles. It affects people from different age groups, professions, and social situations. An editorial preface published in the Annals of the New York Academy of Sciences [65] stated that “stress fully pervades our life and influences us as individuals, communities, and humanity".

7.1 What is Stress?

Hans Seyle defined stress for the first time in 1936 [235] as “A Syndrome produced by diverse Nocuous (noxious) Agents". Later in 1973, in a more elaborate paper “The Evolution of the Stress Concept" he defined stress as “the non-specific response of the body to any demand made upon it" [234]. So, any kind of demand, whether it is physical such as a pin prick, or emotional, such as a sad or happy moment can elicit to a stress response from our body. Subsequently, Mason et al in 1976 showed that psychological stress such as fear, threat, or challenge, produced different reactions (for eg. cortico-steroidal secretions) than physical stress such as heat, hunger, and pin prick.

In this work we focus primarily on psychological or mental stress and its corresponding physiological reactions. We define stress as an imbalance between the demands upon a person and their ability to meet them. Studies have shown that the perception of stress can affect the health outcome differently than the actual stress itself. The difference between actual stress on an individual and the ability of the person to cope with the stress is referred to as “Perceived Stress". Studies have shown that the perception of stress can affect the health outcome differently than the actual stress itself [166].

7.2 Effects of Stress

It is normal for the human body to be exposed to a limited amount of stress. Unless the stress is prolonged and chronic, the human physiology is capable of handling and recovering from it. However, being exposed to continuous high stress can have negative effects on a person’s physical and mental well-being. It has been strongly linked to numerous chronic health risks, such as cardiovascular disease, diabetes mellitus, obesity, hypertension, and coronary artery disease. It is also a contributory cause for unsuitable human behaviour, failure, and psychological breakdown among people from different age groups, professions, and culture, and has become a growing concern in workplaces around the world.

Stress has been widely linked to mental workload which is defined as the relationship between the demands of a task and the capacity of the employee [151]. High mental workload is one of the most frequently cited causes of work-related stress and increased level of [169]. A high perceived workload, along with high perceived stress has been shown to increase the level of fatigue [169] among employees and even increase the risk factors of cancer[144].

While it is possible to identify the source of physical stress or severe acute psychological stress, subtle and chronic stress due to continuous workload is more challenging to detect. Because of this most people are unaware of the level of stress in their lives. By the time people decide to seek medical help they are already in the advanced stages of stress induced exhaustion or are suffering from some noticeable ailment. To prevent this, there is a need for early detection of stress.

Stress causes the activation of the sympathetic nervous system and trigger the human “fight-or-flight response" [145]. This response, also called as the "acute stress response" was first described by Walter Cannon in the 1920s as the theory that animals (including humans) react to threats by activating specific physiological actions in the sympathetic nervous system. This activation is to prepare the body to either fight the threat, or run away from it. The immediate action is an increase in the secretion of epinephrine (adrenaline), norepinephrine (noradrenaline), and cortisol.

Adrenaline increases heart rate, elevates blood pressure and boosts energy supplies. The effect of increase of norepinephrine is to heighten alertness. These hormones lead to physiological changes to deal with the threat - they increase oxygen availability by increasing heart rate and breathing. They increase blood flow to the organs essential to fighting the threat such as heart, brain, and muscles and restrict blood flow to organs which are non-essential to deal with the stress response, such as the skin and digestive system. Cortisol, also called the “stress hormone", increases blood glucose level and enhances the brain’s glucose absortion.

The human body is quite capable of handling bursts of short-term stress. Once the stressor or the threat is removed, the homeostatic process of the body decreases the hormone secretion, and returns the bodily functions to their baseline. However, the body cannot sustain such bursts of energy for a long term - the increase is heart rate, blood pressure, and blood glucose level over a long period of time can disrupt the body’s normal processes and can lead to weight gain, sleep loss, digestive problem, hypertension and cardiovascular problems.

7.3 Detection of Stress

Psychologists, clinicians and researchers have developed and tested techniques for early detection of stress and workload. While some techniques such as the application of questionnaires for stress detection has been popular for over thirty years, other techniques such as the mobile and wearable devices for stress detection is fairly new. We discuss these techniques as under:

- **Questionnaires**

  Since the early 1980s psychologists have used validated questionnaires for detecting stress. Psychosomatic medicine often relies on questionnaire-based assessment of perceived stress [96]. Self assessment questionnaires are also widely used for evaluating stress coping strategies.

  Emotion Regulation Questionnaire Emotion regulation refers to the process that individuals use to feel, express, and control the emotions they experience in their daily lives [113]. The emotional reactions to stressful events entail emotion regulation [263]. Different individuals use different emotion regulation strategies which can affect the way they experience and deal with stress. It has been shown that individuals who use *antecedent-focussed* strategies such as *Cognitive Reappraisal*, experience and cope with stress differently than individuals who use *response-focussed* strategies like *Expression Suppression*.

- **Visual Features**

  Emotion theories state that non-verbal features or visual cues include features such as facial expression, eye gaze, posture, and head and body movements can be highly indicative of the mental state of a person. Spontaneous facial expression can provide accurate information about emotional experience. In a study published in 1978 Ekman and Friesen presented the facial action coding [85] scheme to identify six basic emotions (happiness, disgust, surprise, sadness, anger, and fear) based on facial expressions shown by people across cultures. Hirokazu and Kazuhito [176] used a technique called Facial Expression Spatial Charts (FECS) to analyze the effect of stress on facial expression of subjects. Kumano et. al in 2009 did a study on smile to indicate and assess emotion and attention in interpersonal meetings. In 2005, Kapoor and Picard [153] studied facial expressions and postural shifts to classify children's affective state, including frustration while solving puzzles.

- **Speech Features**

  Vocal indications of emotional stress have been widely studied in literature due to the ease of collection of speech data compared to other forms of signals. The first study of vocal expressions and emotion was done by Charles Darwin [74] who concluded that there is a direct correlation between the emotional state of a person and his vocal communicative actions. Research in speech characterization has shown that analysis of voice patterns based on vocal tract, prosodic, and glottal source can be used for identifying emotion and stress in voice [229, 229, 163].

- **Neurological Features**

  Since the theories of stress detection derive from the broader field of cognitive thoeries for emotion detection, several works have used electroencephalography (EEG), magnetic resonance scan (MRI) and functional magnetic resonance imaging (fMRI) for stress detection. Khosrowabadi et al [154] proposed a brain computer interface (BCI) for classifying EEG correlates of chronic mental stress. This study showed the various brain region activation changes with respect to the mental stress level.In [120] Hamid et al used Perceived Stress Scale and EEG Power spectrum recording to detect human stress level. Lanius et al in [165] used fMRI to study the activation of the thalamus for patients who suffer from post traumatic stress disorder.

- **Physiological Signals**

  Physiological signals such as galvanic skin response (also known as electrodermal activity), heart rate variability (HRV) and skin temperature have been used to recognize stress and workload under different experimental conditions. Galvanic Skin Response (GSR) has been a widely representative signal under various settings ranging from driving scenarios [131] to working in an office [67] or a call center [134]. Heart rate variability has been effective in tracking and measuring both stress and workload. Jovanov et al. [148] demonstrated the use of a distributed body area network for recording Heart Rate Variability (HRV) from different points on the body to quantify stress level. Cinaz et al. [67] used a wearable heart rate monitor to track mental workload for controlled experiments using present during an office workday. In [243] Soga et al. physiological responses are studied to evaluate the intensity of generated stress induced by mental workload. By watching out for risk factors such as sudden blood pressure drops [95] or abnormal heart rate [241] it is possible to provide early life saving warnings.

- **Smart Phone Signals**

  In recent years smart phones have increased in their computational powers and sensing capabilities. A mobile phone has become an integral part of our lives and is a powerful sensing machine which can provide a deep insight into its user's lifestyle. Just looking at the call and message logs provides a view into his or her social life. Communication channels like Bluetooth and Wifi can also act as passive sensors for determining where we are, who is in the user's vicinity. The selection of the most frequently used applications provides a look into the user's personality. Most smart phones come equipped with embedded location (GPS), and motion (Accelerometer and Gyroscope) sensors which can be used to determine the motion profile of the user. These sensors can report the daily activity level of the user. Longitudinal monitoring can provide deep insight into both the physical and mental well being of the user.

7.4 Challenges in Stress Detection

Stress is a fuzzy and highly subjective concept, and it is difficult to quantify it. One of the major hurdles in identifying and preventing stress in life is that the same stressful conditions does not always generate the same stress response. There is emperical evidence that supports the view that some subjects are more resilient to exposure of stressful events in daily life than others. While for some a certain stressor may invoke a highly negative stress response, for others the effect can be quite negligible. Yet, for others, research has shown that stress can even improve performance [81]. There are individual difference in the cognitive variables and personality traits of people which need to be taken into account while judging their response to stress. A widely held opinion in the current psychological literature says that resilience to stress is related to personality traits and adaptive life-styles including well developed feelings of self-awareness and styles of emotion regulation.

Using laboratory and controlled experiments for measuring stress response of individuals may thus be confounded by their emotion regulation and resilience in real life conditions. To identify how an individual responds to stress, there is a need to observe the individual's stress response under ecological settings. However, on-the-go stress recognition has its limits. Its not possible to use visual features for continuous recognition - its not practical to continuously have a camera pointing at a person outdoor. The possibility of using neurological features is also limited by the fact that EEG devices are cumbersome to wear. However, the use of physiological and smartphone signals do offer such an opportunity for in-the-wild stress monitoring.

The first attempt at recognizing stress in the wild was done by Healy and Picard in 2005 for measuring stress during real world driving tasks [131]. They used a complex setup of various sensors (one electrocardiogram on the chest, an electromyogram on the shoulder, a chest cavity respiration sensor, and two electrodermal activity sensors) (See Figure. 7.1) which connected to a computer to monitor the changes in the physiological signals and facial expressions of subjects as they navigated different road conditions. They were able to recognize three different levels of stress (low, medium and high) with a 97.4% accuracy. However, their setup was cumbersome and not practical for everyday monitoring.

Hong et al. [172] in the *StressSense* project proposes to use human voice for continuous unobtrusive stress monitoring. They demonstrated that it is possible to identify stress from a person's vocal features during job interview, marketing and natural reading scenarios. They achieved accuracies of 81% and 76% for indoor and outdoor scenarios respectively. Hernandez et al. [134] demonstrated that using a wearable electrodermal activity senror its possible to identify the stress of call center employees with an accuracy of upto 73.41%. Muaremi et al. in [194] in 2013 achieved an accuracy of 61% by combining smart phone features with heart rate features extracted from a chest based wearable heart rate monitor.

Continuous ambulatory monitoring of stress in naturalistic settings

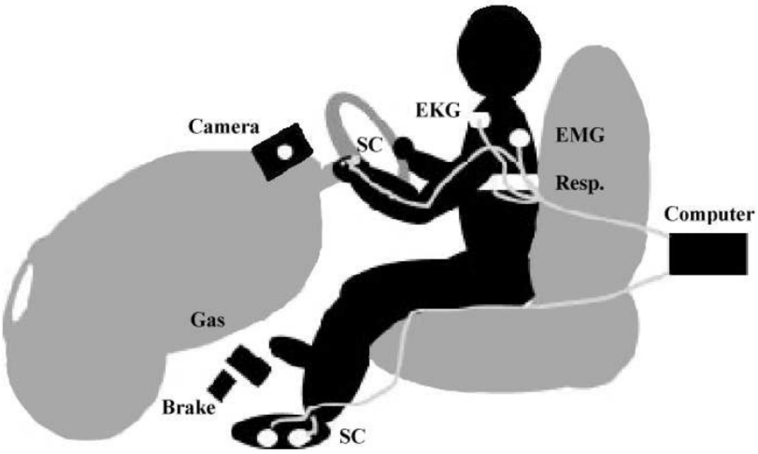


Figure 7.1: The subject wore different sensors which captured the physiological responses as the subject. Healy and Picard 2005 [131].

suffers from a few challenges:

- It is difficult to obtain the stress related annotations from subjects in real life: Stress perception of an event changes or is often forgotten after a stretch of time;
- Physiological signals are highly susceptible to noise from motion;
- A system for stress recognition based on a single physiological signal is not robust.

We tackle these challenges through the Health Analytics (HEAL) intelligent personal agent platform. The HEAL mobile personal agent regularly and continuously elicits information from the user. Also it uses activity recognition algorithms which provides additional information about the user's context.

We hypothesize that rather than using a single physiological feature for stress recognition, combining various physiological features such as heart rate variability along with electrodermal activity and skin temperature will provide better recognition of the user's stress level. Also, since stress responses are person specific, we also need to take into account the characteristics of the user. Therefore we employ a multi-dimensional strategy which consists of a combination of various covert (physiological) and overt (patient annotations) signals for a robust stress recognition system which performs well under noisy real-world scenarios.

7.5 EXPERIMENTAL DESIGN

The HEAL platform was used in this study. In this preliminary study for detection of stress, five healthy subjects (three males and two females, between ages of 30 and 45) holding regular desk jobs were recruited. The subjects were selected after an initial prescreening interview with a psychologist to eliminate the possibility of underlying mental condition such as hidden hypertension which might affect the study. The protocol for this research study was approved by the ethics committee of the Università degli Studi di Trento. The subjects were provided with the Italian version of the emotion regulation questionnaire by Balzarotti et al [31] as described in chapter 3. It is a ten-item self-report questionnaire which uses the cognitive reappraisal and expression suppression scales to evaluate an individual's tendency to regulate his or her emotion and respond to stress.

Subsequently, each subject was provided access to the (HEAL) intelligent personal agent platform.

7.5.1 Protocol and Data Collection

Each subject was provided with the HEAL intelligent agent application, and an Empatica E3 wristband. As a part of the protocol each subject used the HEAL Platform for a period of seven days (five working days and a weekend) for 8-10 hours, every day from morning till evening. Thrice during the day (once in the morning, at lunchtime, and at the end of the day) the subjects used the HEAL Agent Application to report their anticipated and perceived stress and workload status. The answers were selected from a six-point Likert scale which ranged from “Very Peaceful" to “Very Stressful" for perceived stress; and “Completely free" to “Very Busy" for perceived workload. The subjects were also asked to take regular text and voice notes annotating activities, and events such as consumption of alcohol, nicotine and any other caffeinated beverage during the day. At the end of the day, they noted a brief textual or verbal description of their day, and using the online platform, reviewed, added or edited any information provided.

A total of 206 hours of sensor data was collected. The subjects annotated 61 instances of reported stress, and 60 instances of reported workload using the application.

7.6 EXPERIMENTS AND RESULTS

In most stress-related studies, workload is taken as the cognitive demand of the task. In such controlled experiments, the mental workload is increased by varying task complexity, and its effect on the stress response of the subject is observed. Our goal is however, to study and predict stress and workload individually under naturalistic settings. For our experiments we observed a low correlation (pearson = 0.58 p-value < 0.05) between perceived stress and perceived workload.

In this section we discuss the initial preprocessing of the collected data to minimize noise. Then we discuss the feature extraction and classification experiments.

To detect the stress state and workload of the subject we need to extract useful information-bearing features from the different signal streams. We extract and combine features from the different physiological and inertial sensors on the Empatica Wristband and iPhone with the ***personal features*** of the subject. The personal features of the subject are the features extracted from the motion profile of the subject, the emotion regulation questionnaire and the daily subject feedback.

7.6.1 Data Analysis Pipeline

The complete end-to-end data analysis pipeline is presented in Figure 7.2. The pipeline consists of five layers:

1. **Input Layer:** The input layer consists of three input streams - 1) physiological and accelerometer signals from the user's wristband 2) accelerometer and gyroscope signals from the user's smartphone 3) the notes from the users which comprises of answers to questionnaires and annotations of events.

2. **Preprocessing Layer:** The preprocessing layer performs the activity recognition from the smartphone motion sensor data. This information is used for removing artifacts from the physiological signal which can affect the stress recognition algorithm.

3. **Artifact Removal Layer:** The artifact removal layer uses the activity data from the above preprocessing layer to generate cleaner physiological signal streams.

4. **Feature Extraction Layer:** The feature extraction layer extracts features from the various signal streams.

5. **Classification Layer:** The classification layer uses the features extracted above to distinguish between the stress and workload levels.

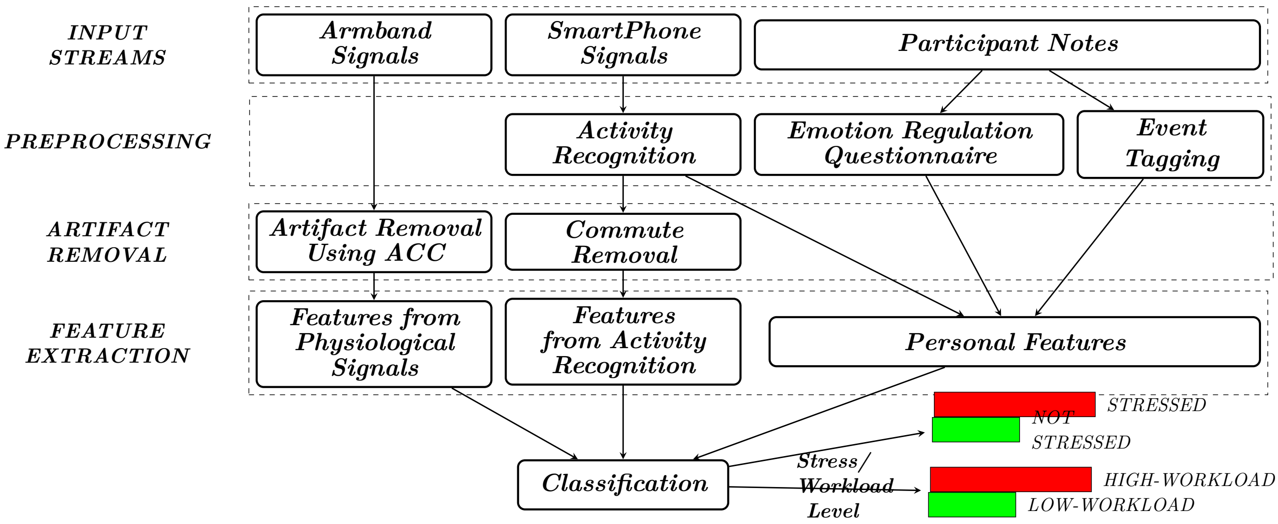


Figure 7.2: End-to-end signal processing pipeline & classification system which shows the steps starting from the signal acquisition to the classification.

7.6.2 Data Preprocessing

Wrist based physiological sensing devices are affected by artifacts due to local or gross motion, so they need to be preprocessed before feature extraction. As a first step we recognize the activity profile of the subject, then use this for artifact removal and signal estimation.

Activity Recognition: The activity recognition model is learned using the approach, data and features of [108] as explained in Chapter 6. For the activity recognition task, as described before, we use the onboard inertial sensors of the user's iPhone. We identify six activities - *Walking*, *Standing*, *Sitting*, *Driving*, *Travelling by bus*, and *Travelling by Train* and segment our data with continuous labels. In chapter 6 we show that combining the features from accelerometer and gyroscope signals provides a good recognition accuracy at lower sampling rates. In order to conserve the battery of the iPhone we use a sampling rate of 5 Hz. To reduce the noise of the recognition, for every 3 minutes, we take the majority of the recognized activities and label the 3 minute segments as belonging to that activity class.

7.6.3 Artifact Removal

Commute Detection: We combine the three activity classes *Driving*, *Travelling by bus*, and *Travelling by Train* into a single class *"commute"*. Research has shown that the length and quality of commute can contribute to stress. City commuting can be extremely stressful. Factors such as traffic congestion, how crowded the bus or train is, what is the noise level of the commute, can all affect the stress level of an individual. Hence the duration of commute becomes an important factor for stress recognition. Stutzer and Frey in a 2008 study [253] conducted in Germany showed that greater commuting time decreased life-satisfaction. However, due to lack of other grounding signals, further analysis of stress during commute can be quite challenging. We only use the total commute duration as a feature to create a daily **Activity Profile** of the subject.

Using the above algorithm, for the collected user data, we recognized 88.5 hours of sitting, 16.6 hours of walking and 20.3 hours of standing and 79.3 hours of commute. All these factors contribute to the **personal features** of the subject. We consider the periods for which the subject was either walking, sitting or standing for our stress and workload recognition tasks.

Artifact Removal from Wristband Signals: Local fidgeting of the wristband, and motion artifacts arising out of posture and activity are common sources of artifacts experienced in a wearable monitoring system. From user feedback we learnt that a new wrist-based device can cause local discomfort for the first couple of days which may increase nervous fidgeting. This fidgeting introduces unwanted noise in the physiological signals which can confound the recognition algorithm. We use a heuristic approach for identifying and removing these local artifacts. Whenever we observe abrupt changes in the accelerometer of the wristband which are concurrent with abrupt changes in all the physiological signals, we classify that segment as a local artifact. We therefore remove the next 30 seconds of the data from the time of the artifact initiation from our subsequent processing.

7.6.4 Feature Extraction and Machine Learning

Physiological Features - We extract features from the Electrodermal Activity (EDA), Blood Volume Pulse (BVP), Inter-Beat-Interval (IBI), and Skin Temperature (SKT) signals recorded from the Empatica E3 wristband. The Electrodermal activity which refers to the variation in the electrical properties of the skin due the variable activation of the sweat glands, is arguably one of the most useful indicators of sympathetic arousal. We extract features from both the skin conductance level (SCL) (the slow moving tonic EDA) and the skin conductance response (SCR) (rapid short-lasting change in the EDA). First we remove the baseline for each subject and normalize the values to lie in the [0,1] range. Then we extract a total of 24 features from the SCL and SCR for each session. Features extracted from the EDA included statistical features such mean, standard deviation, maximum, and minimum. Characteristic features extracted from the skin conductance responses includes the number and sum, minimum and maximum of the areas under the peaks of the SCRs exceeding a threshold and the sum of the duration of the SCRs.

We smooth the PPG data provided by the Empatica E3 wristband to derive the Blood Volume Pulse (BVP) signal, and extract 8 statistical features from this BVP signal stream. The Empatica E3 wristband reports the Inter Beat Interval (IBI) at a discrete rate. The IBI or the N-N interval, is the time difference between two normal sinus beats. The heart rate can be calculated from this signal as $HR = 60/IBI$.

Heart Rate Variability (HRV) is an important measure of stress and mental activity of a person. We extract well explored HRV features such as SDNN (Standard Deviation of the N-N interval), pNN50 (percentage of consecutive N-N intervals which differ by more than 50 milliseconds), RMSSD (root mean square of the successive difference of N-N interval) [192, 200, 67] among others, extracting a total of 10 features from this IBI signal stream. We extract a further 8 statistical features from the Skin Temperature (ST) signals.

Inertial Sensor Features - The Empatica wristband has an accelerometer to calculate the tri-axial acceleration. We also have at our disposal the accelerometer and gyroscope channels from the iPhone. From each of these channels these we extract 10 statistical features (including mean, SD, min, max, number of peaks per minute).

Personal Features - The personal features for each subject comprise of three sets of features. The first source is the activity profile of the user. This consists of the duration of the commute of the user, along with the duration of sitting, standing, and walking for each session. The second set of features is derived from the Emotion Regulation Questionnaire which the subjects had filled in. We calculate the Emotion Suppression (ES) and Cognitive Reappraisal (CR) scores for each subject. The third source is the event tagging done by the subjects. We consider the counts of the beverage, caffeine and alcohol intake which was reported by the subjects using the agent application.

Machine Learning - To perform classification, we formulate our daily stress and workload recognition as two independent binary classification tasks. Stress is classified into two classes as “Stressed" and “Not Stressed", and workload as “High Workload" and “Low Workload". We use a “Leave One Subject Out" (LOSO) cross validation scheme for all classification tasks. We perform classification on both individual and combined signal streams. For signal stream combination we perform a feature level fusion

Signal Streams	Avg F-measure
BVP	0.74
GSR	0.79
IBI	0.69
ST	0.44
Inertial	0.56
BVP + GSR	0.82
IBI + BVP + GSR	0.89
IBI + BVP + GSR + Inertial	0.82
IBI + BVP + GSR + Personal Features	**0.91**

Table 7.1: Classification results for individual and best combinations of features for **perceived stress** using Random Forest Algorithm with LOSO evaluation.

Signal Streams	Avg F-measure
BVP	0.63
GSR	0.44
IBI	**0.73**
ST	0.37
IBI+BVP	0.69
Inertial	0.72
IBI+Inertial	**0.78**
IBI + BVP + Inertial	0.71
IBI + Inertial + Personal Features	0.75

Table 7.2: Classification results for individual and best combinations of features for **perceived workload** using Random Forest algorithm with LOSO evaluation.

of the physiological features with the features from the activity profile and the personal features of the subjects.

We use the Random Forests algorithm for all classification tasks. The Random Forests algorithm, which was introduced by Breiman in [48], is an ensemble learning method and is a conglomeration of tree-based classifiers. The results of classification of the level of stress and workload are reported in Tables 7.1 and 7.2 respectively. We report the classification results for individual signal streams and the results for the best combinations. We observe that a combination of physiological and personal signals give the highest F-measure for the stress classification task. Combining the physiological features with person specific features, we arrive at a high value of F-measure of 0.91. However, adding inertial features leads to a drop in performance. From Table 7.2 we observe that individually, features extracted from the IBI stream are the best indicators of perceived workload (0.73). Combining them with the features from the inertial sensors provide an improvement (0.78) in classification performances. The personal features which were indicative of stress, do not provide any improvement in the workload classification task.

7.7 Conclusion

In this chapter we demonstrate a method to continuously track and measure stress and workload in naturalistic settings which can be deployed for on-the-go acquisition and monitoring of subjects. We show that the performance of the combinations of weak signal streams is greater than that of individual signals for predicting stress and workload.

Stress is a contributing factor for hypertension - continuous high stress can weaken the immune system and lead to cardiovascular diseases including hypertension. There is a need for early automatic detection of stress. Using a combination of physiological, and smart phone signals along with profile data can enable this early detection, and subsequent intervention to implement stress reduction.

8

Detection of Hypertension

The main and final goal of this thesis is the early detection of hypertension. The early diagnosis of essential hypertension can support the prevention of cardiovascular disease, a leading cause of death. As explained in the earlier chapters, the traditional method of identification of hypertension involves periodic blood pressure measurement using brachial cuff-based measurement devices. These devices, however, require careful set-up for each measurement, and they are not generally suitable for use outside clinical settings. While doctors have advocated the use of ambulatory blood pressure measuring devices for continuous monitoring, their adoption is still lagging. Recently, electronic blood pressure monitoring devices have made regular home based blood pressure monitoring easier. However, they are mostly used by the elderly who are already suffering from the disease, or by people who are aware of their risk of hypertension. There is a need to develop techniques for continuous unobtrusive monitoring and detection of hypertension which can be deployed on a large scale.

In this chapter we explore alternative ecological methods of detection of hypertension. In chapter 7 we already demonstrated that combining multiple signal streams from wearable devices and smart phones can be used to detect stress with a high accuracy. In this chapter we explore how these physiological signals from wearable devices can be used for detecting hypertensive patients. We also explore the relationship between perceived stress and hypertension to confirm that perceived stress is an indicator of hypertension.

8.1 Use of Wearable Devices for Hypertension Detection

In recent years, wearable devices with multiple connected sensors have made healthcare ubiquitous and patient-centric. Unlike ambulatory blood pressure monitoring devices, most wearable devices are comfortable and aesthetic, and are being rapidly adopted by the general population. Devices like the *Basis Armband* [14], *Microsoft Band* [13], *Empatica Embrace* [2] amongst others, are capable of measuring multiple motion and physiological signals such as Electrodermal Activity (EDA), Skin Temperature (SKT), Blood Volume Pulse (BVP), and Heart Rate. Such devices have opened up a great unprecedented opportunity for continuous remote monitoring and predictive diagnosis for various medical conditions. Researchers have achieved a wide level of success in the detection and monitoring of people suffering from stress, epilepsy, bipolar disorder, and sleep apnoea [107, 210, 213, 219] using wearable sensors.

However, one major drawback of using wearable sensors is the presence of artifacts which can contaminate the signal. Artifacts can be caused due to movement of the device arising out of body motion, or pressure on the device due to clothing, nervous fidgeting by the person wearing the device, or even vasoconstriction due to cold weather [237]. Hence there is a need to develop effective signal processing methodology for artifact removal before these signals can be effectively used for experiments in detection of hypertension. In this chapter we describe a robust signal processing pipeline as used in [109] to improve the quality of the signals.

Previously while recognizing stress from physiological signals, we observed that combining multiple signal streams improve the accuracy of the recognition of stress under real-life scenarios. In this chapter we apply the same approach to explore how individual and combinations of various physiological signals can be used to detect hypertensive patients.

8.2 Stress and Hypertension

High life stress, especially occupational stress is considered to be an important factor that contributes to the development and persistence of hypertension [255]. People with occupations which are designated as more stressful (air traffic controllers [68], nurses [98], etc.) have a higher resting blood pressure and an increased risk of developing hypertension.

Non-occupational stress like living in high stress urban areas [25] or in communities which have experienced terrorist attacks [137] can also elevate blood pressure and increase the risk of incidence of hypertension and cardiovascular ailments. Research suggests that psychological distress and psychosocial factors may be associated with the pathogenesis and the prognosis of cardiovascular events[59, 125, 230, 270, 152]. The results reported in [222] suggest that anxiety is also significantly associated with hypertension. In this study we explore the differences in stress responses between normotensive and hypertensive subjects.

8.3 Study Objectives and Design

An observational and non-interventional pilot study was designed to investigate the following:

(1) Investigate the differences in the stress response of normotensive and hypertensive subjects.

(2) Create a signal processing pipeline for reducing artifacts in the physiological signals recorded from wearable devices.

(3) Identify differences in the features of physiological signals (especially HRV) of normotensive and hypertensive subjects.

(4) Create and test a machine learning pipeline for automatic detection of hypertensive patients.

(5) Understand the attitude of patients towards continuous ambulatory monitoring of physiological signals using an intelligent personal agent and a non-intrusive wearable wristband.

The study sample consisted of fourteen hypertensive patients (8 male and 6 female) and 12 normotensive controls (6 male and 6 female) between the age of 30 and 65. At the time of the study the hypertensive patients were receiving treatment at the ***Centro Ipertensione Ospedale Molinette*** in Turin, Italy. The healthy control (normotensive) subjects were selected to be of similar demographics as the patients and were checked by a psychologist to rule out masked hypertension or any other underlying health problem that might affect the study. The institutional ethics committee of Azienda Ospedaliera Città della Salute e della Scienza di Torino and the ethics committee of the Università degli Studi di Trento approved the present research study. The patients suffered from Essential Hypertension(EH) with no underlying malignancies. At the time of this study they had been diagnosed with EH grade I or II controlled by therapy, without organ damage (average age 49,2, average body mass index (BMI) of 25,43 Kg/m2, mean office arterial pressure 127.57/83.57, average heart rate 73.5, average number of drugs 1.5). Patients performed blood pressure monitoring for 24 hours (ABPM) to rule out "white coat effect".

8.4 Study Protocol

The data collection protocol for the study was the same for both groups of subjects (both patients and controls). Each of the participant was provided with an Empatica E3 wristband, and an iPhone with an installed HEAL intelligent agent application as described in chapter 5. The HEAL agent continuously acquired physiological signals and stress and lifestyle related annotations throughout the duration of the experiment and securely transmitted them to the HEAL analytics cloud.

8.4.1 Psychological Assessment and Surveys

At the beginning of the study we conducted psychological evaluation of the hypertensive (patient) and normotensive (control) groups to identify differences between them. One of the hypotheses of our study is that individual differences in coping strategies toward stress is an indicator of hypertension and this difference can be observed between the two groups of subjects (controls and patients). This hypothesis is grounded on the observation that people respond to stressful events in different ways, depending on the life event and on the regulatory styles they adopt. To overcome the vagueness of the concepts of stress and psychosomatic factors, psychological models have been designed to account for coping and emotion regulation.

Emotion regulation is a process by which individuals modify their emotional experiences, expressions, and physiology and the situations eliciting such emotions in order to produce appropriate responses to life events [114]. Two underlying strategies have been proposed as primary factors of the emotion regulation process; they are reappraisal and suppression. Reappraisal is a strategy which acts before the activation of emotional response, while suppression is a strategy that occurs when an emotional response has already been deployed. Which strategy a person employs is an indicator of their resilience. It has been suggested that the suppression strategy may require some effort to manage the emotional response thus reducing the individual cognitive and affective resources.

For investigating the possible differences in emotion regulation styles between the hypertensive and normotensive groups of subjects we used the Italian version of the Emotion Regulation Questionnaire [31]. Moreover, for assessing the possible differences in individual stress perception, we administered the Perceived Stress Scale [265] Questionnaire. During the psychological interview with each subject, the psychologist also assessed the occurrence of long term stress events before the onset of the disease [138].

8.4.2 Data Collection

Each subject wore the Empatica E3 wristband for a period of seven days (five working days and a weekend) for a duration of 8-10 hours from morning, till evening. The signals continuously recorded were:

a) Electrodermal Activity (EDA)

b) Blood Volume Pulse (BVP)

c) Skin Temperature

d) Inter Beat Interval (IBI)

e) Tri-axial accelerometer signal from the wristband

f) Tri-axial accelerometer and gyroscope signals from the iPhone

Thrice during the day, the participants used the mobile application to report the following stress state:

a) Anticipated Stress and Workload Reporting

b) Perceived Stress and Workload Reporting

Using the HEAL agent application, the participants also noted down the caffeine (tea, coffee, cola), nicotine, and alcohol consumption during the day. They were also encouraged to take frequent voice and text notes. At the end of the day, they noted a brief textual or verbal description of their day, and using the online platform, reviewed, added or edited any information they wanted.

A total of 2356 hours (1203 hours from hypertensive patients and 1154 hours from normotensive control subjects) of sensor data was collected. We obtained a total of 533 instances of stress annotations from hypertensive patients and 457 instances from normotensive subjects. The total counts of the stress annotations are shown in Table 8.1.

	Anticipated Stress	Reported Stress
Normotensive	233	224
Hypertensive	273	243

Table 8.1: Number of Stress Annotations from each group of subjects

8.5 Differences in Stress Response between Normotensive and Hypertensive Subjects

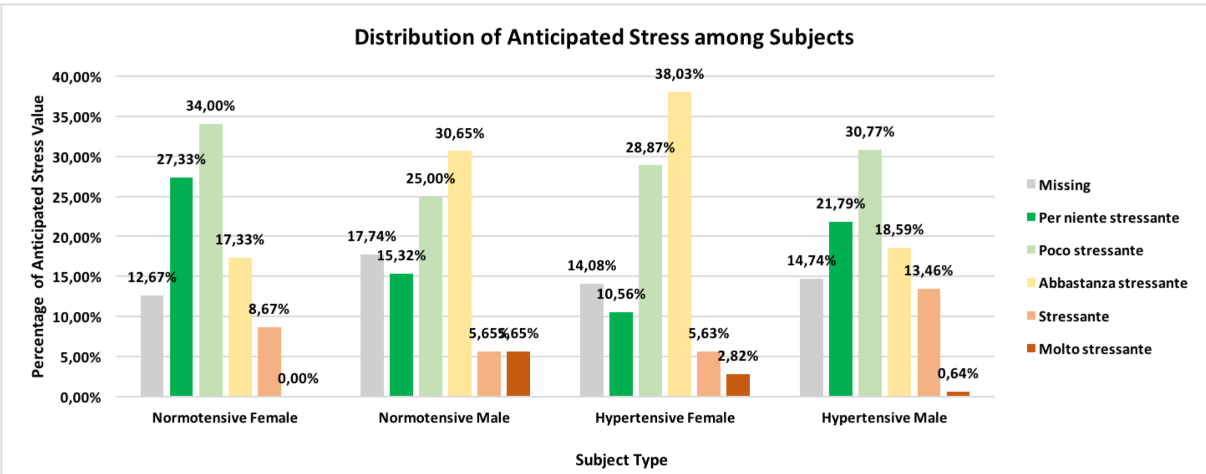


Figure 8.1: Distribution of anticipated stress annotations of Normotensive and Hypertensive Subjects

Analyzing the anticipated and perceived stress values of the normotensive and hypertensive subjects, we observe that the distributions of their stress responses differ. Overall hypertensive subjects recorded a higher stress value (abbastanza stressante, or stressante, or molto stressante) for anticipated stress 39.5% of the time compared to normotensive subjects who reported values in this range only 33.9% of the time. For perceived stress, hypertensive subjects reported a higher value 31.8% of the time as compared to normotensive subjects whose perceived stress value lay in this range 28.7% of the time.

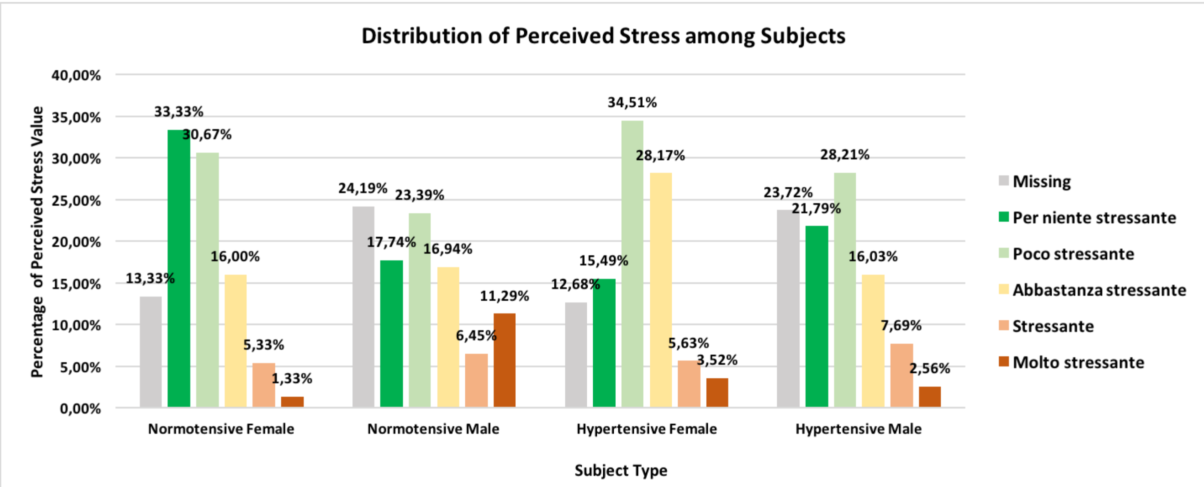


Figure 8.2: Distribution of reported stress annotations of Normotensive and Hypertensive Subjects

The differences in stress responses were more pronounced in the female subjects. We find statistically significant differences for both anticipated and perceived stress annotations between normotensive and hypertensive female subjects. For female hypertensive subjects anticipated stress values were in the higher range of the stress scale (abbastanza stressante, stressante, and molto stressante) 46.3% of times, while this was 26% for female normotensive subjects ($p = 0.003$). For perceived stress this difference was equally significant - 37.3% of the perceived values were in the higher range for hypertensive female subjects compared to only 22.67% for normotensive females ($p = 0.003$). We did not find any significant differences between the responses of the male subjects.

8.6 Signal Processing Pipeline for Physiological Signals

Physiological signals collected from everyday ecological settings suffer from a variety of artifacts and noise. The Empatica E3 reports Electrodermal Activity (EDA) and Skin Temperature (ST) at 4 Hz, Photoplethysmograph (PPG) data at 64 Hz, and tri-axial acceleration at 32 Hz. Prior to any analysis, the signal streams need to be preprocessed for artifact removal and normalization.

When a subject wears the E3 device, there is initial local perspiration because of the contact of the device with the skin. This causes an initial rapid increase in the EDA signal which requires a few minutes to stabilize. The Empatica E3 photoplethysmograph sensor also calibrates itself before it can start reporting the PPG data. Hence for every session, we remove the first five minutes. Then for each individual signal we preprocess it to decrease the amount of noise. For the EDA and Skin Temperature (ST) we first use a low pass Butterworth filter. Then we detrend the EDA to remove the temporal low frequency drift.

8.6.1 Estimating an Accurate Interbeat-Interval

Photoplethysmography data is highly susceptible to motion artifacts and this can lead to detection of unrealistic values of heart rate. The Empatica E3 performs on board signal processing to remove motion artifacts from the PPG signal [106]. However, we observed that the reported PPG data still contained certain local motion artifacts, which conditioned the resulting signal entropy. In the physiological signal literature, different methods have been proposed to remove artifacts from PPG data for the derivation of Blood Volume Pulse (BVP) and Heart Rate signals. Adaptive filters schemes [238], (e.g. NLMS, RLS), [276] and smoothing algorithms (e.g. Moving average filters) [186] support the accelerometer subtraction for noise removal.

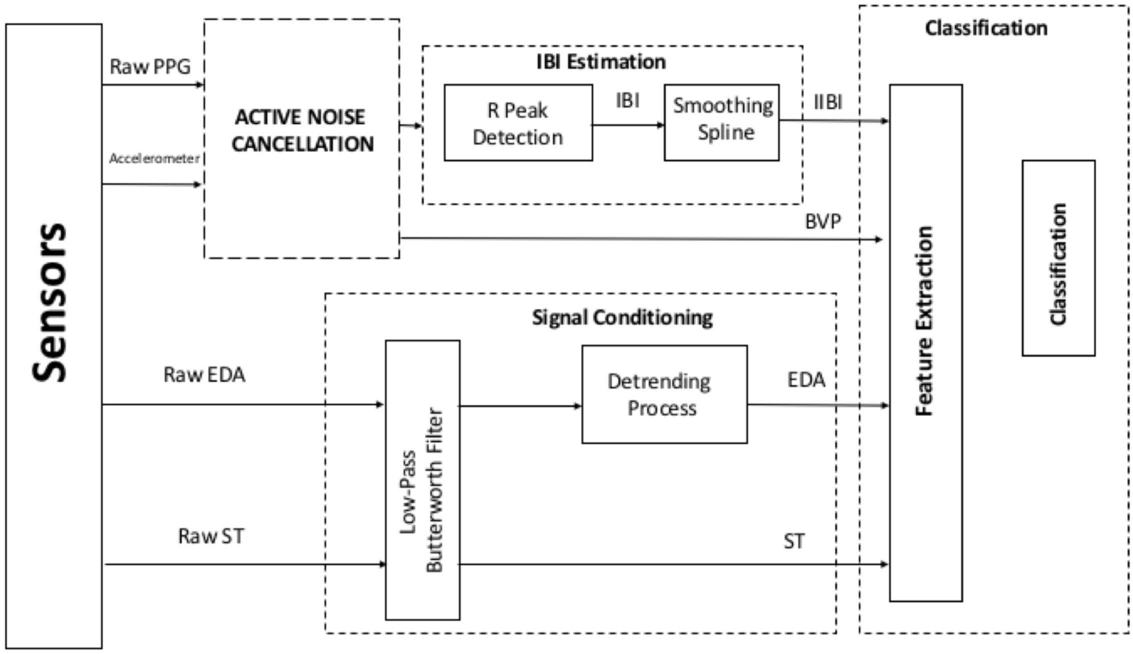


Figure 8.3: Pipeline for Hypertension prediction from Wearable Devices. We define four different blocks, a) Active noise Cancellation, b) R-peak IIBI estimation c) Signal conditioning and d) Classification

We process the PPG signal with the Active Noise Cancelation method as proposed in [121] to derive a clean IBI signal. This method consists of a Least-Mean-Squares (LMS) adaptive algorithm, used to minimize the error with respect to the desired filter impulse response coefficients. In this chapter we use the same approach as in [121], and define a $32nd$ order FIR passband filter as our desired response defined by $[0.5-5]Hz$ bandwidth.

Due to the lack of a ground truth for the Inter-Beat Interval (IBI) signal for the Empatica E3, we evaluate our algorithm on the publicly available TROIKA dataset [277] proposed in the 2015 IEEE signal processing cup, which closely mimics real-life motion activities. This dataset is composed of 5 minute long treadmill trials, performed by 12 different subjects. The signals recorded are PPG, accelerometer and include an ECG ground-truth. Each 5 min trial is divided into 6 different exercise tasks as follows: 30 seconds - rest (1-2 km/h), 1 min - Walking (6-8 km/h), 1 min - Running (10-12 km/h), 1 min - Walking (6-8 km/h), 1 min - Running (10-12 km/h) and finally 30 seconds - rest (1-2 km/h). This dataset consists of a collection of photoplethysmograph and Accelerometer data along with ground truth electrocardiogram (ECG) data collected We evaluated our algorithm Active Noise Cancellation and prediction methods on the TROIKA data and obtained an absolute error of 12.1% and a relative error rate of 8.9% for Heart Rate estimation.

Consequently we apply this methodology to our dataset for estimating a continuous Inter-Beat-Interval signal. With the filtered BVP signal, we detect the R-peak positions that are above 50% of the BVP signal amplitude. For each detected consecutive R-peak pair, we calculate the time difference between them and detect any variation along the entire BVP signal. Thus when we detect a new R-peak according to the above criterion, we update the inferred IBI value. Finally we run a smoothing spline algorithm, in order fix the resultant IBI signal and avoid undesirable harmonics related with IBI discontinuities. This signal is commonly called interpolated-IBI (IIBI) [186]. We can see both these signals in figure Fig. 8.4.

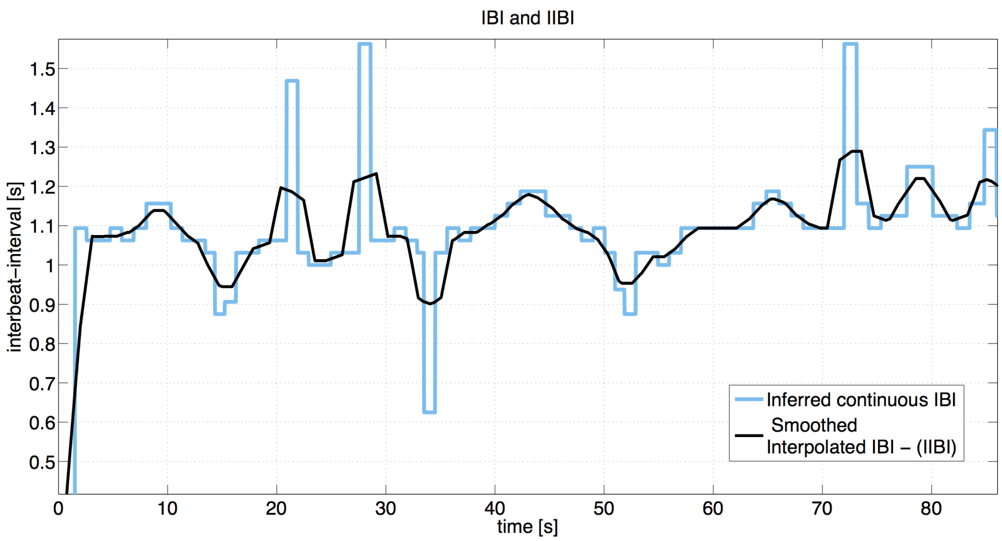


Figure 8.4: Example for inferred IBI and Smoothed IIBI.

8.7 Analysis of HRV

From the inferred Inter-beat-Interval signal we calculate heart rate variability. Heart rate variability (HRV) is a popular and useful noninvasive tool to assess cardiac autonomic regulation. Heart rate Variability is used to describe the variations in the instantaneous heart rate or the RR intervals. A reduction of heart rate variability has been linked to a poor prognosis of several clinical conditions. In 1965 Hon and Lee [141] observed a decrease in the inter-beat interval value of HRV as a signal of fetal stress. A reduction of HRV has been accepted as a correlate stress [37], and in several cases is associated with increased mortality and morbidity. Reduced HRV has been shown to be correlated with an increase in the risk of cardiovascular mortality [201, 259].

Heart Rate Variability is an important physiological factor for people suffering from hypertension. Studies have reported the reduction of HRV in hypertensive patients when compared to normotensive subjects [143, 231]. Continuous monitoring of HRV has been recommended for patients suffering from essential hypertension.

In this study we analyzed the time domain features of the Heart Rate Variability - the normal-to-normal R-R interval length (R-R interval), the standard deviation of the R-R intervals (SDNN), the Root Mean Squared Standard Deviation (RMSSD) and the average heart rate. All these features have been shown to be lowered in hypertensive patients [231] as compared to normotensive subjects. As shown in Table 8.2, all these parameters are lowered in hypertensive patients compared to the normotensive subjects.

From Table 8.2 we observe significant differences in the HRV features of normotensive and hypertensive subjects. R-R interval, RMSSD, and SDNN was significantly reduced in case of hypertensive patients compared to normotensive subjects. While this reduction was observed in both genders, it was more pronounced in the male group. The mean difference between the mean R-R interval of female hypertensive patients and normotensive

	All		Male		Female	
	Normo tensives	**Hyper tensives**	**Normo tensives**	**Hyper tensives**	**Hyper tensives**	**Hyper tensives**
Heart Rate (bpm)	66.3 ± 5.8	72.4 ± 7.6	66.4 ± 5.4	74.1 ± 4.9	66.18 ± 6.3	69.10 ± 10.19
R-R interval (ms)	911 ± 84	838 ± 95	909 ± 78	813 ± 56	915 ± 93	885 ± 12
RMSSD (ms)	29.4 ± 3.7	26.8 ± 4.5	29.9 ± 3.1	26.7 ± 3.8	28.7 ± 4.3	27.1 ± 5.6
SDNN (ms)	49 ± 12	39 ± 13	51 ± 11	39 ± 12	45 ± 12	39 ± 16

Table 8.2: Heart Rate Variability Features between Normotensive and Hypertensive Subjects. We can observe a marked lowering of RR-Interval and SDNN in Hypertensive Subjects. We also observe that Heart Rate is elevated for Hypertensive subjects than the Normotensive. *All values are significant with p-value below 0.005*

patients was 20 milliseconds. This difference was of 96 milliseconds in the male group.

Elevated Heart Rate has been shown a positive association with mortality [111, 205]. Reduction of heart rate among hypertensive patients should therefore be a goal of anti-hypertensive therapy. In Figure 3 we can see the distribution of the heart rates of the hypertensive and normotensive subjects. We observe that the average heart rate for hypertensive patients is higher than that of normotensive subjects. The mean heart rate of the hypertensive group was found to be 72.4 beats per minute, while that of the normotensive control group was 66.3 beats per minute. This elevation is marked in case of male patients, with make hypertensive subjects having a mean heart rate of 74.1 beats per minute, compared to 66.4 beats per minute for normotensive males.

The evaluation of the data collected from the psychological assessment showed some interesting differences between subject and control group. Table 3 reports in the first column the different areas that have been explored during the psychological structured interview. The psychologist asked the subjects to describe their family life: as we expected, the participants from the patient group were more available in describing their private life, including the details of the history of their disease. In particular, the perception the patients had of their health status was

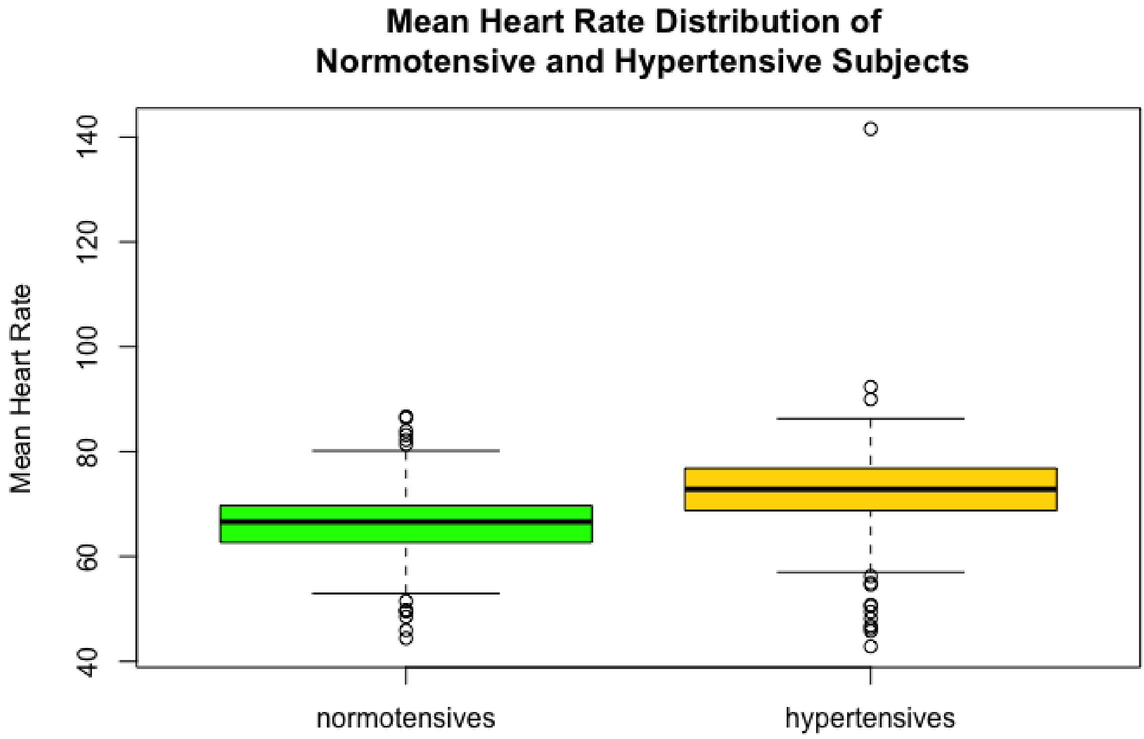


Figure 8.5: Distribution of mean heart rate for the Normotensive and Hypertensive Subjects

somewhat unrealistic. Notwithstanding their being well controlled by therapy, and without organ damage – both conditions were among the inclusion criteria of the study, they reported a perception of being affected by a severe disease. Compared to the control group, they also reported a higher value for stressful events in the past six months (Holmes & Rahe scale). In addition, from the interviews it was revealed that at the time of the onset of their disease the patients had been exposed to varying levels of life-changing events. While some of them has been confronted with loss events, like divorce, illness or death of a relative, others had experienced potentially positive events like job change, and newborns in family. As for the personality profiles, from the psychological observation it resulted that in the patient group 8 out of 14 subjects could be classified as Type D personalities vs 2 out of 12 in the control group. Finally, the analysis of the personality traits showed that in the patients' group traits such as neuroticism and consciousness were more represented.

8.8 Analysis of Electrodermal Activity

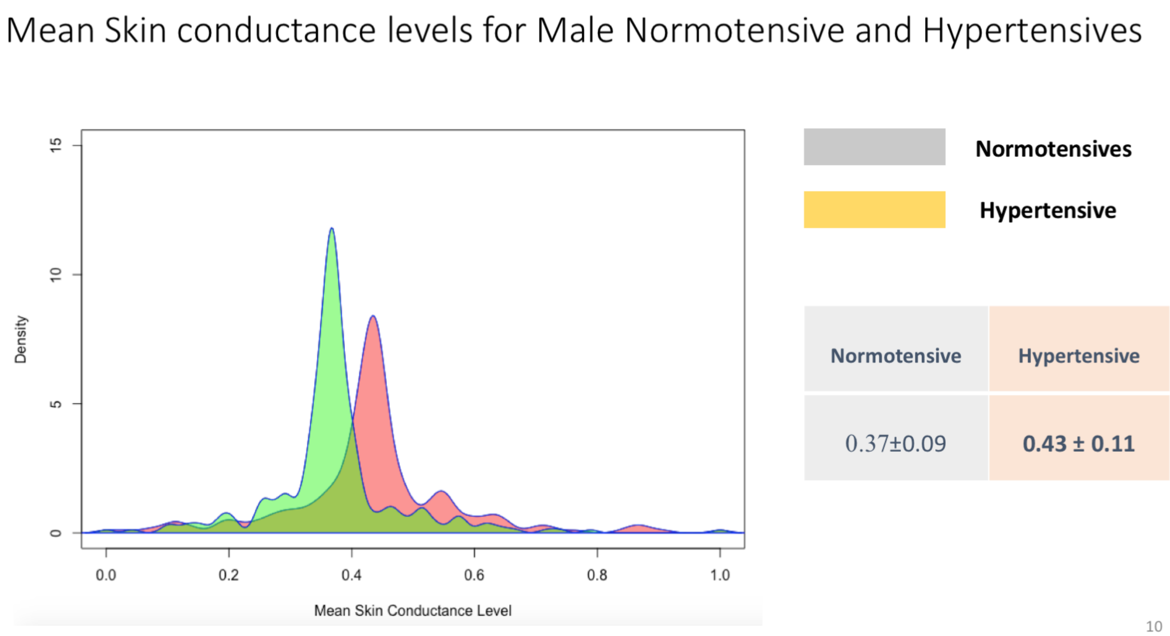


Figure 8.6: Distribution of mean skin conductance level (SCL) for male Normotensive and Hypertensive Subjects

Electrodermal activity (EDA) is an important indicator for stress. In this study we observed that features of EDA can also be used as indicators for hypertension. We studied the normalised skin conductance level (SCL) which is the skin conductance level in the absence of any external stimuli obtained from durations where the electrodermal activity did not show any skin conductance response (SCR). We observed significant difference in the normalized mean skin conductance level (SCL) between the hypertensive and normotensive groups. Since we did not have any ground truth for the type of external stimuli which the subjects experienced during their daily lives, the study of skin conductance responses (SCRs) for making conclusions was avoided - however, we observed that features from SCR can provide additional benefit to the classification algorithm. For our comparison, in order to account for person specific differences, we normalised the SCL. We observe that the mean normalized SCL of normotensive controls was 0.37 as compared to 0.43 for the hypertensive group. We observed a significant different in the SCL levels in both male and female groups.

Figure 8.6 shows the density distribution of the skin conductance level of the normotensive and hypertensive males while the 8.7 shows the same for the female groups.

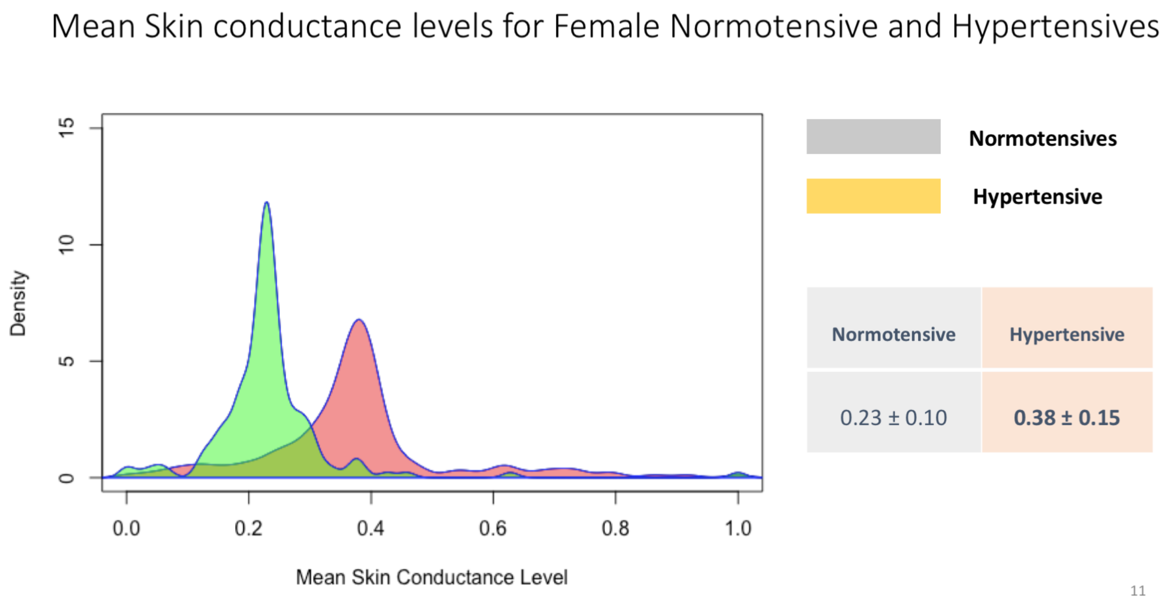


Figure 8.7: Distribution of mean skin conductance level (SCL) for female Normotensive and Hypertensive Subjects

8.9 Automatic Detection of Hypertension

One of the goal of this work is to automatically identify hypertensive patients. For this we

8.9.1 Feature Extraction and Classification

Feature Extraction

The window size of the physiological signal not only affects the quality of the hypertension detection algorithm but also determines the duration for which a subject needs to be monitored for such a task. We experimented with different window sizes to discover the optimal window for continuous monitoring of physiological signals and how the performance varies. We extracted features for window sizes ranging from 15 minutes to 2 and a half hours. For the feature extraction we consider all the signals. We extract features from the preprocessed Electrodermal Activity (EDA), the Skin Temperature (ST) signals as well as the cleaned Blood Volume Pulse (BVP) and Interpolated Inter-beat-interval (IIBI) signals which were derived from the PPG data. The raw inter-beat interval data provided by the Empatica E3 was sparse and noise and for this work we did not use that signal. Here we discuss the various features extracted from the individual physiological signal streams.

From the Electrodermal Activity (EDA) we extract statistical features (mean, SD, min and max) for each session. We also extract the counts of the startle responses (instantaneous changes in response to external stimuli) of the EDA signal and their average rise and fall durations. The duration and amplitude of a the startle response of the Electrodermal Activity has been shown to be highly correlated with sympathetic activation of a person, and its long term monitoring can be useful in detecting subjects who may be hypertensive . In total we extract 24 features from the EDA signal. We further extract 17 more features form the cleaned Blood Volume Pulse Signal and 8 features from the Skin Temperature Signal.

From the Interpolated Inter-Beat Interval (IIBI) we extract 17 features from the time and frequency domain. The time domain features of IIBI are related to the parasympathetic and sympathetic baroflex function and hence are indicative of Heart Rate Variability. Hence, we extract the maximum and minimum of Heart Rate, RMSSD (root mean square of the successive difference of NN interval), SDNN (Standard Deviation of the NN interval), pNN50 and pNN30 (percentage of consecutive NN intervals which differ by more than 50 and 30 milliseconds respectively). We also derive frequency domain features as indicated in [124, 140]. These features are related to the sympathovagal balance index and indicative of sympathetic and parasympathetic neural activity. We also extract the ratio of the Low Frequency and High Frequency values (LF/HF ratio), and the statistical features given by each frequency range, (e.g. LF and HF: mean, variance, max and min peaks).

Machine Learning

For distinguishing between hypertensive and normotensive subjects, we perform a Leave One Subject Out (LOSO) cross-validation classification. Since each test fold contains instances from either a hypertensive subject or a normotensive subject, we compute the final global confusion matrix by combining the individual classes per fold for each subject.

True Positive comprises of all hypertensive subjects classified as hypertensive. True Negative comprises of all the normotensive subjects classified as normotensives. False Positive is all normotensives classified as hypertensives, and all the hypertensives classified as normotensives makes up the False Negative class.

We perform classification with both individual and combined signal streams. A feature-level fusion of the different physiological signal streams is done before running different classification tasks. We perform feature normalization to scale all features to the range [0,1]. We evaluate the performance of five different classification algorithms: K-Nearest Neighbours, Naive Bayes, Decision Trees, SVM with Linear kernel, and two ensemble learning algorithms - Adaptive boosting and Random Forest. The ensemble based classifiers outperform the other classifiers for both individual and fusion of features, with Adaptive Boosting performing

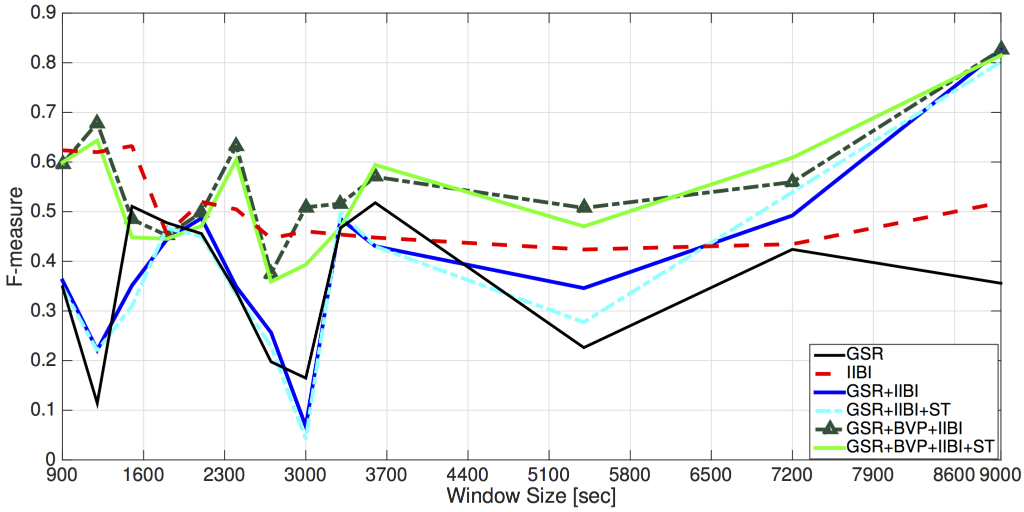


Figure 8.8: Effect of the different sampling window sizes (in seconds) for the Adaboost classifier for different Feature combinations.

the best. Adaptive Boosting (Adaboost) is a meta-learner that uses greedy search on a linear combination of weak classifiers to generate a single composite strong learner. We use AdaBoostM1 which is a binary classification algorithm.

When considered separately, individual signal streams have low classification accuracies, with Blood Volume Pulse having the highest F-measure of 0.62. However, combination of features of different signal streams significantly improves the classification results. EDA-IIBI and EDA-BVP-IIBI combinations providing the best discrimination between hypertensive and normotensive subjects. We observe that we are able to achieve a high F-measure of 0.83 using a combination of features from the BVP, EDA and IIBI signals.

The length of the feature extraction windows as discussed in section 8.9.1, affect the classification results. From Figure 8.8 we can observe that the best F-measure is obtained at a window size of two and a half hours (9000 seconds). The classification results can be seen to improve with increase in the signal window.

Table 8.3 summarizes the best performance results which are obtained for a 9000 seconds (two and a half hour) window for the various classifiers.

SIGNAL	Adaboost	RandomFor	SVM
BVP	0.62	0.64	0.59
EDA	0.36	0.44	0.25
IIBI	0.52	0.49	0.33
ST	0.50	0.55	0.53
BVP+EDA	0.52	0.60	0.41
BVP+IIBI	0.63	0.56	0.51
BVP+ST	0.68	0.65	0.59
EDA+IIBI	**0.83**	**0.78**	0.59
EDA+ST	0.48	0.41	0.27
IIBI+ST	0.57	0.52	0.50
BVP+EDA+IIBI	**0.83**	0.72	0.60
BVP+EDA+ ST	0.64	0.53	0.40
BVP+IIBI+ST	0.57	0.57	0.42
EDA+IIBI+ST	0.80	0.71	**0.67**
EDA+BVP+IIBI+ST	0.81	0.76	0.63

Table 8.3: Classification Results (F-measure) for the three best classifiers for different signal combinations for LOSO evaluation for 9000 seconds (2 and a half hour) window. The best performance for each classifier is marked in bold.

8.10 Attitude of Patients Towards Continuous Monitoring

Self monitoring of blood pressure is an effective tool for early detection and management of hypertension. However, self-monitoring can sometimes be difficult and induce added anxiety. This work explores techniques for decreasing the effort involved in continuous monitoring. We explored the patient's attitude towards the protocol for continuous monitoring. The patient-reports are summarized below:

1. Increase in awareness: Seven out of the twelve patients reported that self-monitoring and keeping a diary increased their awareness of daily situations they were usually involved, but that went unnoticed before. For example they became more aware of the total amount of time spent in their cars not only for commuting, but also of moving for shopping, picking the children up from school, etc. In some cases

they observed that some of those activities could have been done by walking. Self-monitoring had also impact on the dietary and smoking habits.

2. Feeling of self-commitment: 9 out of 12 patients reported that during the days of the data collection they were more self-committed with being compliant with the suggestions they had received in the past by their doctors. As an example, they reported that during the data collection they were more precise with the dietary requirements, and with medication intake.

3. Assistance by an Intelligent Agent: 10 out of 12 patients reported that they were interested in the opportunity of “being assisted" by the intelligent agent and wearable device. They did not feel either the agent or the wristband as intrusive, but rather felt them as something that their doctors gave them for taking care of their health throughout their everyday lives.

8.11 Conclusion

In this chapter we demonstrate the use of an intelligent personal agent and a wearable device for hypertension detection. We explore the differences in the stress responses between hypertensive patients and normotensive control subjects. We design and train a complete signal processing and classification system for hypertension prediction. We demonstrate that the proposed computational pipeline which combines several individual signal streams is able to distinguish between hypertensive and normotensive subjects with high accuracy. We find that such an intelligent personal agent is well accepted among patients and can aid in effective management of hypertension.

9

Conclusion

Management of chronic conditions such as hypertension is complex and challenging. Keeping track of blood pressure, stress, activity levels, food and beverage consumption everyday can be a tedious job. For people who are already unwell and suffering, this increases the burden of their disease management. In this thesis we present the Health Analytics (HEAL) intelligent agent platform to reduce challenges faced by the patients suffering from hypertension.

The HEAL platform can monitor both covert and overt signals from a smartphone and a wearable device. The HEAL platform, using the Empatica E3 wearable wristband automatically tracks physiological signals continuously in real-world scenarios. The Empatica E3 is an aesthetic, unobtrusive and comfortable wearable wristband which makes its adoption in daily life easier. The digital multi-modal diary component of the HEAL intelligent agent eases the burden of record-keeping for hypertensive patients. It elicits timely and relevant annotations from patients through structured (questionnaires and lists) and unstructured (voice and text) notes. This information can be aligned with the covert signals to provide grounding for automatically detected events from the signals.

The HEAL platform contains modules for automatic activity recognition under real-world scenarios (Chapter 6). It also contains a pipeline for in-the-wild stress and workload recognition (Chapter 7). Through a pilot study we demonstrate that the HEAL platform can distinguish between hypertensive and normotensive subjects with high accuracy (Chapter 8). The HEAL intelligent agent platform opens up the opportunities for detection and monitoring of a diverse set of chronic conditions. Below we list some of the applications of the HEAL intelligent agent platform:

Monitoring Other Diseases

The technologies developed in this work can be applied for tracking and managing cardiovascular diseases or other chronic conditions. Increasing activity level is an important step for treating different diseases. Automatic classification of activity level as described in Chapter 6 can benefit patients suffering from a broad range of diseases like obesity, diabetes, asthma, and arthritis. Some patients in the hypertension trial reported that the knowledge of the level of activity and time spent driving motivated them to walk more whenever they could.

Physiological signals and digital diaries can be used to detect and monitor diseases such as anxiety, epilepsy and depression. Digital diaries have also been applied for managing and tracking conditions such as eating disorders, obesity, and irritable bowel syndrome. The HEAL platform, which comprises of both these components, can thus be used to simplify the detection, monitoring and management of such chronic conditions.

Monitoring Healthy Individuals

Knowledge of the stress and activity level can benefit healthy individuals. Automatic early detection of stress and workload as described in Chapter 7 can improve the identification of stress factors and help to avoid them. Knowledge of the activity level in general can be used to motivate individuals to get more exercise. Tracking food and beverage intake can increase mindfulness.

The HEAL platform presents techniques which can assist in all these aspects. There is a potential to apply this technology to larger groups of healthy individuals from different communities and job profiles. Observing and learning from a more diverse group of individuals will help to improve the robustness of the stress and activity recognition algorithms.

Long-term Disease Monitoring and Management

In this work we used the HEAL agent to monitor hypertensive patients for a period of 10 days. Even with this short monitoring period, patients reported that using the agent increased their awareness regarding the lifestyle factors which affect their disease. It also increased their feeling of empowerment and commitment towards their treatment regime.

Although these are encouraging results, there is a need for a continued longitudinal study to prove that these positive effects are sustainable and can lead to long-term increase in patient engagement. A short time study did not offer us an opportunity to observe changes in the disease state. A Longitudinal study which can track the progress of the disease over a period of a few months or years can yield useful information that can be used for management of the disease.

Studying Large Diverse Patient Group

The HEAL pilot study for hypertension was conducted with a small group of 14 hypertensive patients (8 male and 6 female) and 12 normotensive controls (6 male and 6 female). While the results were promising, a larger and more diverse study is required to improve the robustness of the algorithms developed in this work. Using the HEAL Application platform opens up the opportunity to conduct such a research. The only requirement for participating in this study is an iPhone and a wearable device (as of now an Empatica E3 - but it is possible to expand to include other devices). The HEAL intelligent agent application is an iPhone application which can be installed in any iPhone anywhere in the world. A patient group with diversity in terms of age, ethnicity and job profile will increase the generality and applicability of the algorithms developed in this research work.

In conclusion, an intelligent agent platform has the potential to change the care-management for chronic conditions. It can help empower and engage patients and improvement detection and subsequent self-management of diseases such as hypertension. Although this work is challenging and there is a need to scale the scope and implementation of this study, the early results are promising and shows the potential for making disease management easier.

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